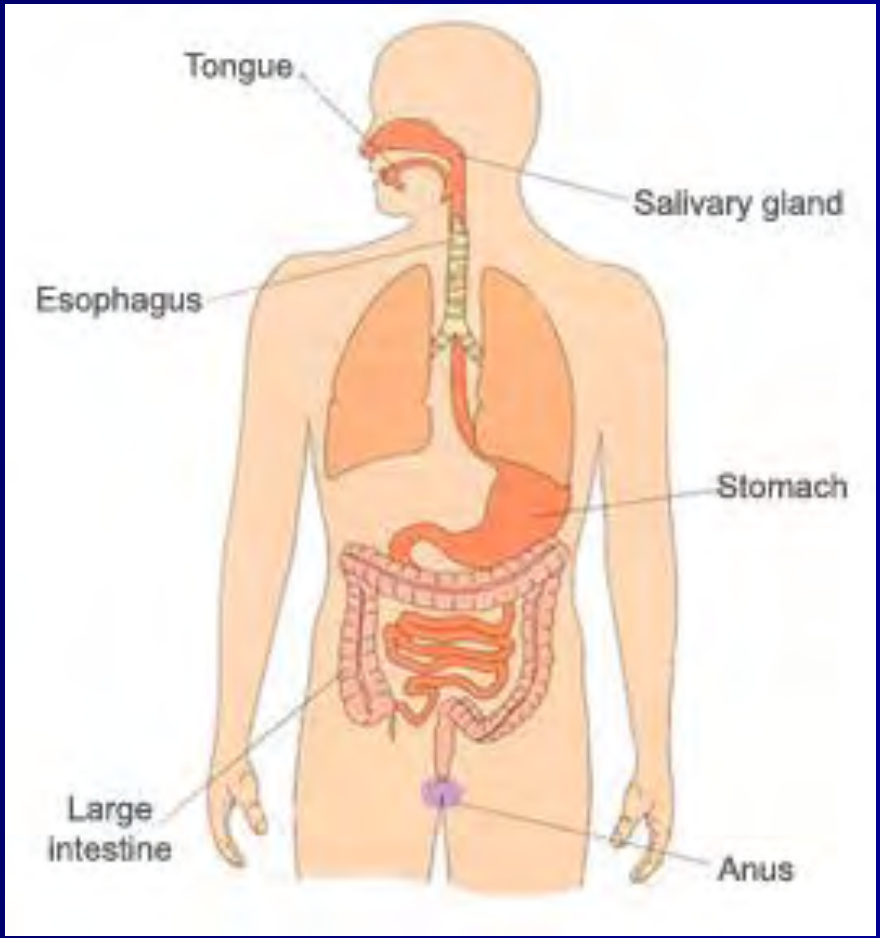
Gastrointestinal Physiology

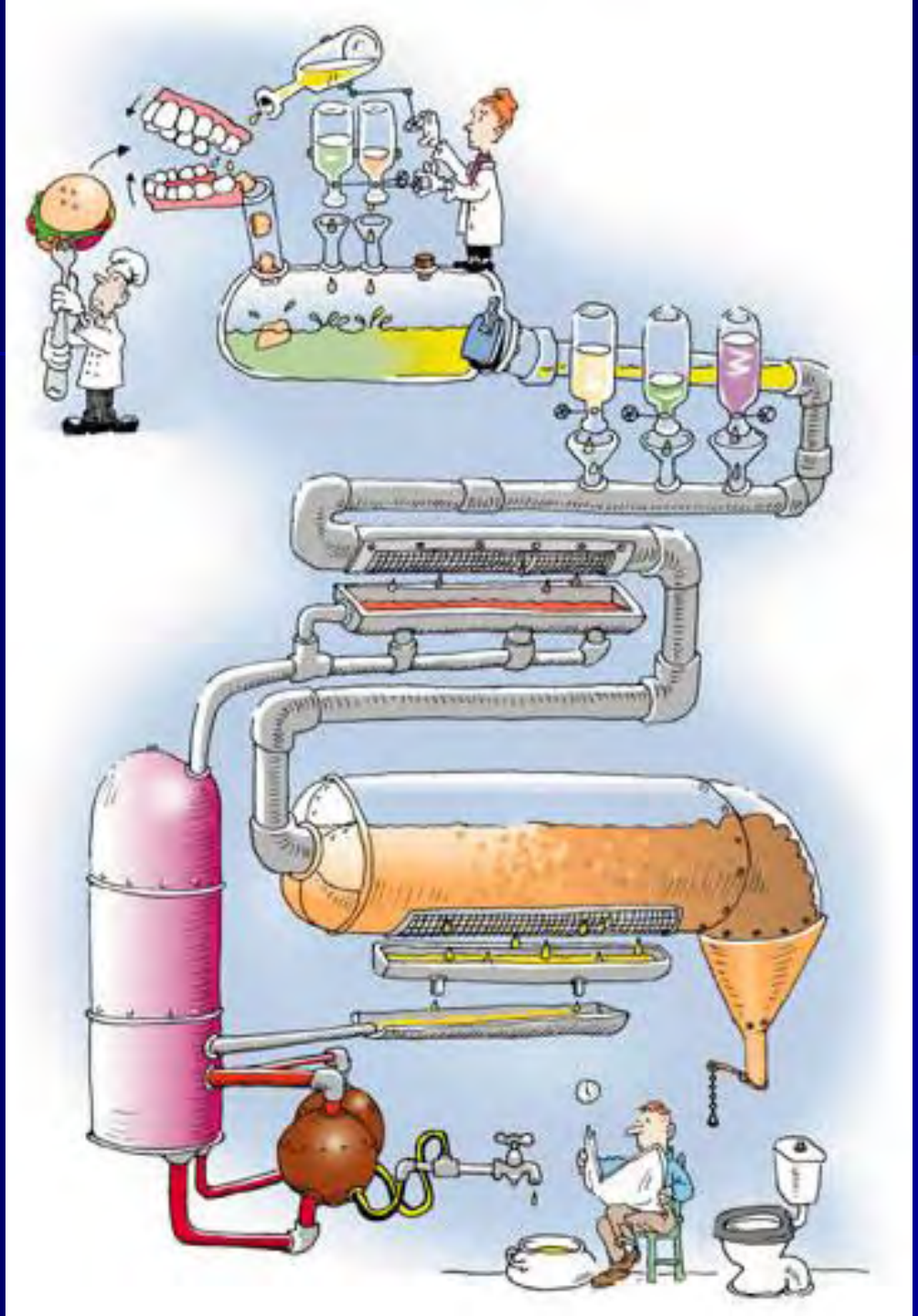


Introduction

- **Digestive system**
  - Alimentary tract (消化道)
  - Digestive gland (消化腺)
- **Digestion**
  - Mechanical digestion （机械性消化）
  - Chemical digestion （化学性消化）
- **Absorption**

Introduction

- Basic processes of digestion and absorption
  - Propulsion （推进） and mixing of food in the alimentary tract
  - Secretory functions of the alimentary tract
  - Digestion and absorption in the gastrointestinal tract



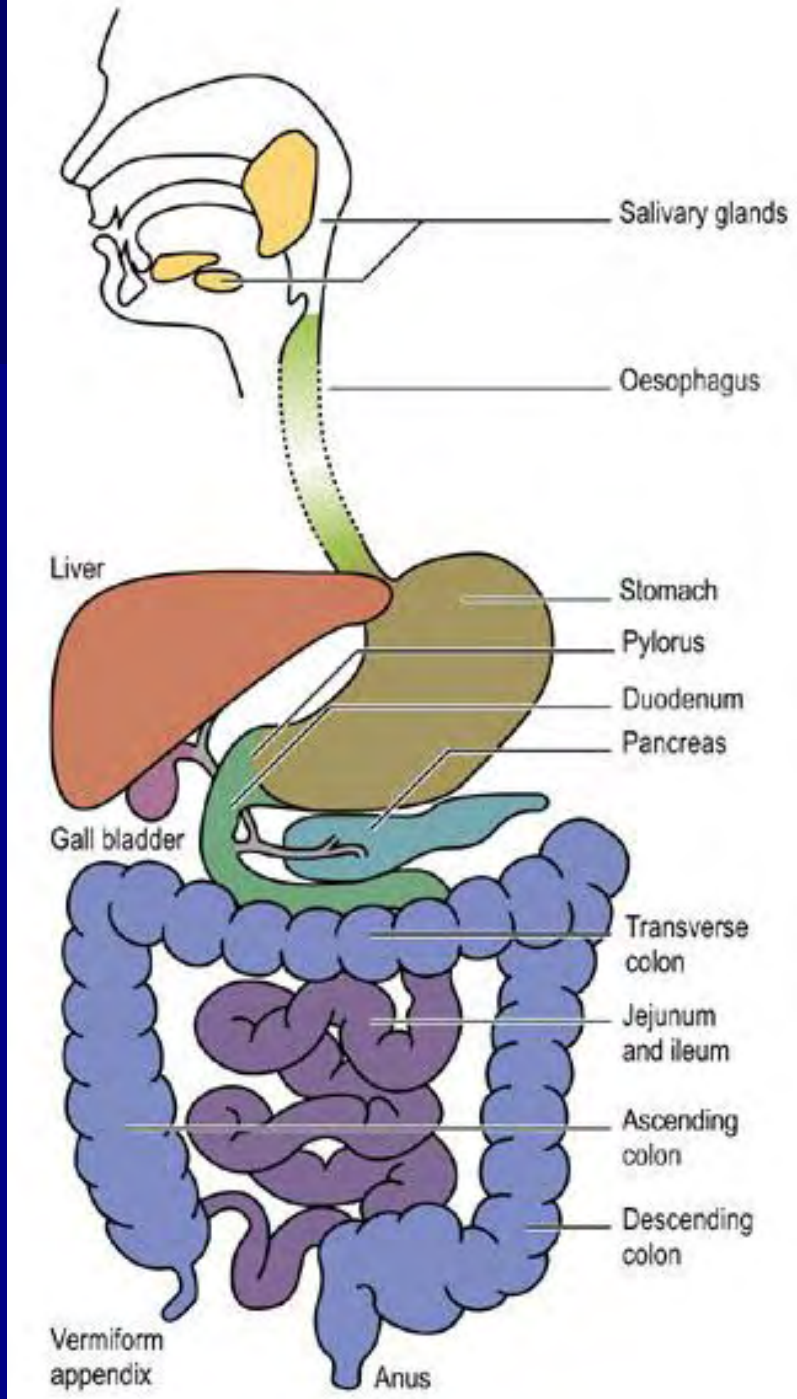
Functions of the digestive system

- Movement: propels food through the digestive system
- Secretion: release of digestive juices in response to a specific stimulus
- Digestion: breakdown of food into molecular components small enough to cross the plasma membrane
- Absorption: passage of the molecules into the body's interior and their passage throughout the body
- Elimination（排除）: removal of undigested food and wastes

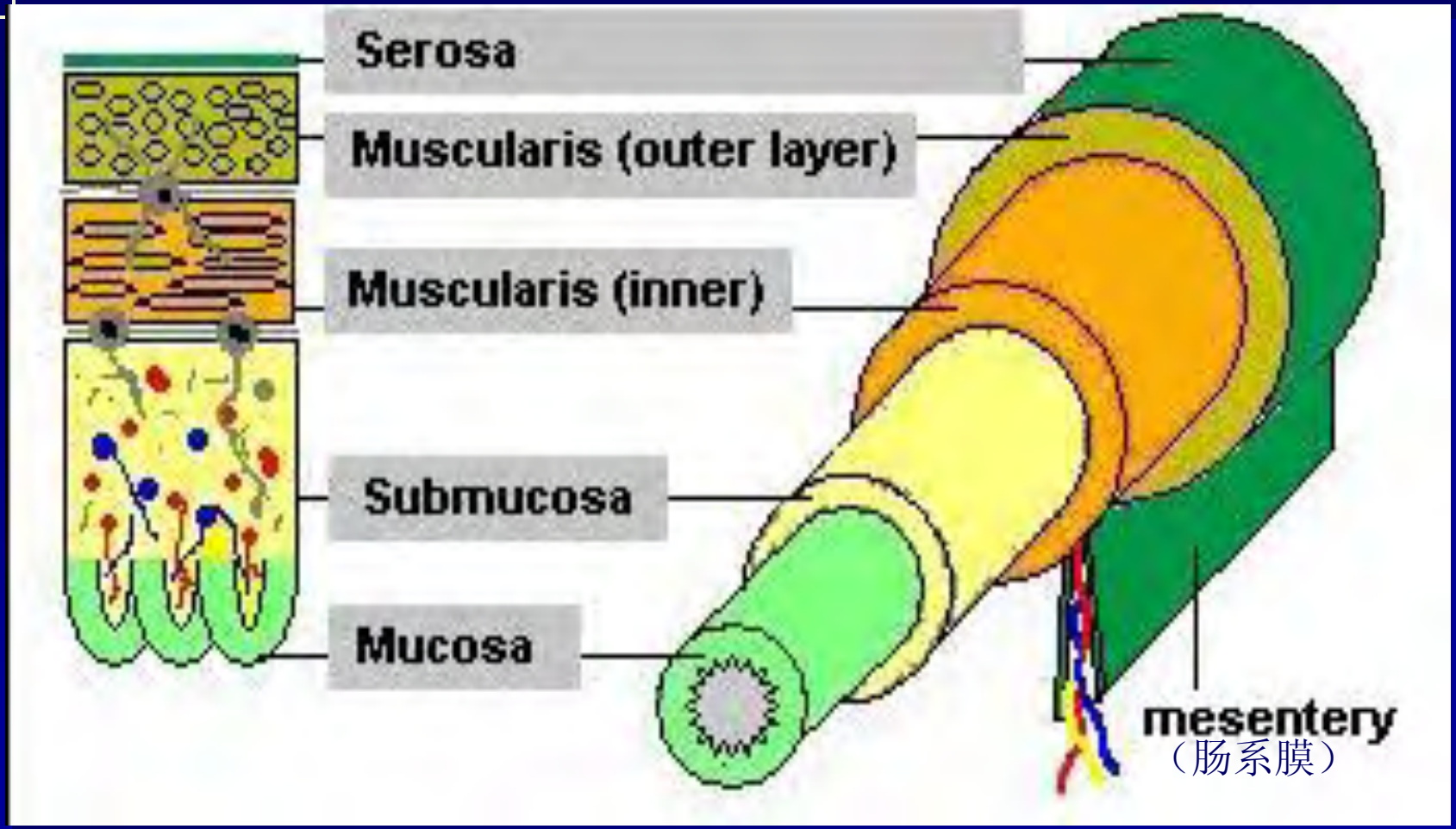
Introduction

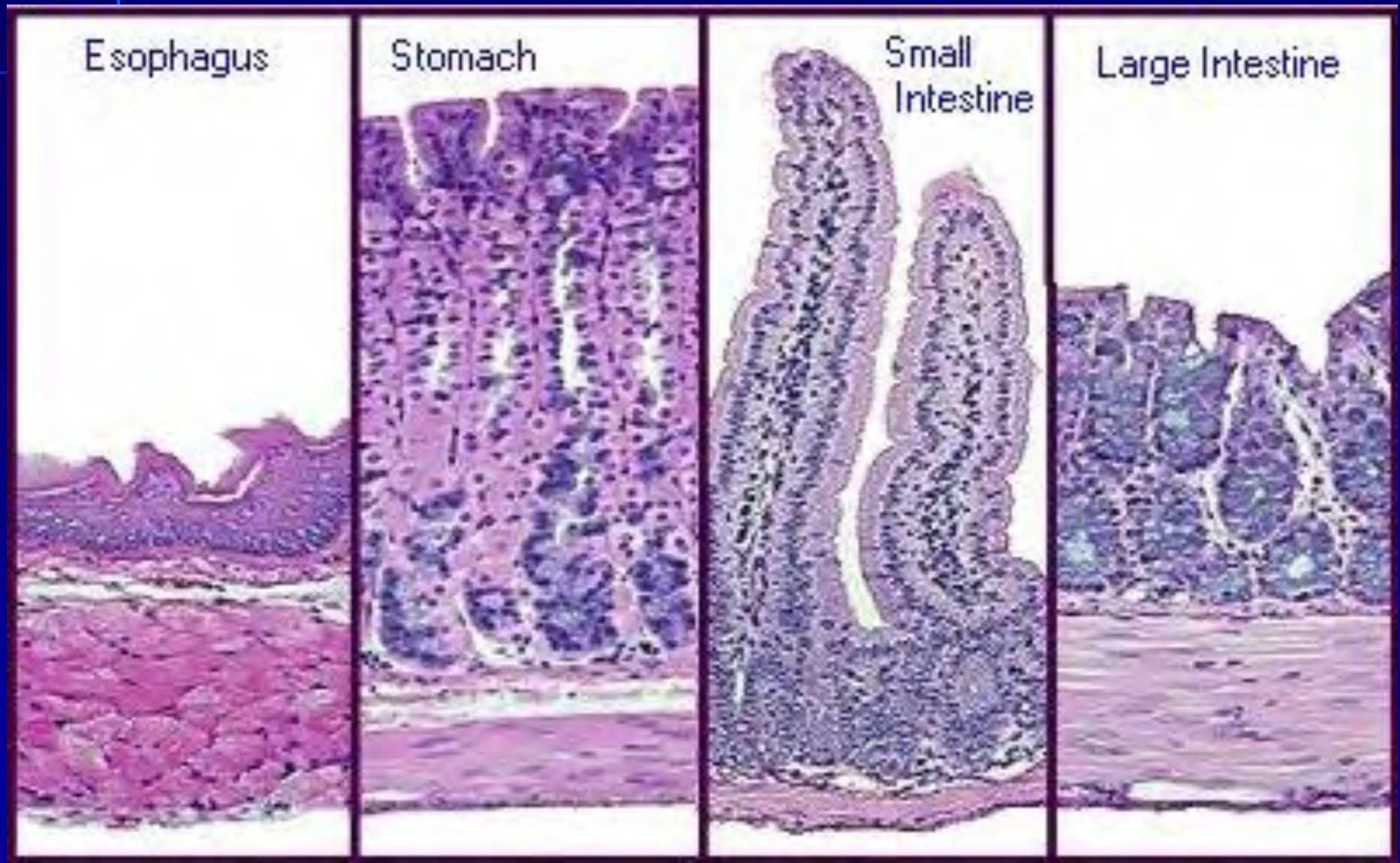
Anatomy:

Components of the digestive system



Structure of the alimentary canal




Esophagus
Stomach
Small Intestine
Large Intestine

General properties of gastrointestinal smooth muscle

- Low excitability
- High distensibility （扩张性）
- Tonic contraction
- Autorhythmicity
- High sensitivity to temperature, stretch and chemical stimulation

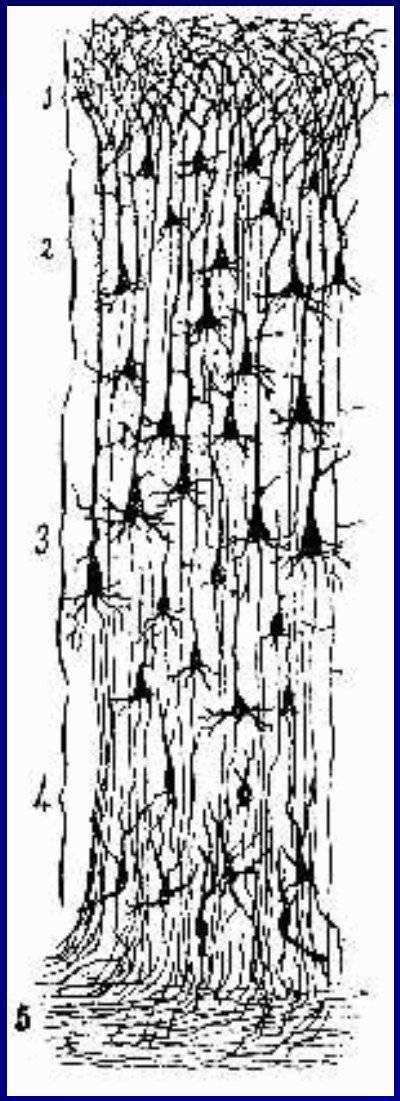
Electrophysiological properties of gastrointestinal smooth muscle

- Resting membrane potential
  - -40~-80 mV
  - Ionic basis
    - Em (selective membrane permeability to K^+, Na^+, Cl^- and Ca^{2+})
    - Electrogenic Na^+-K^+ pump

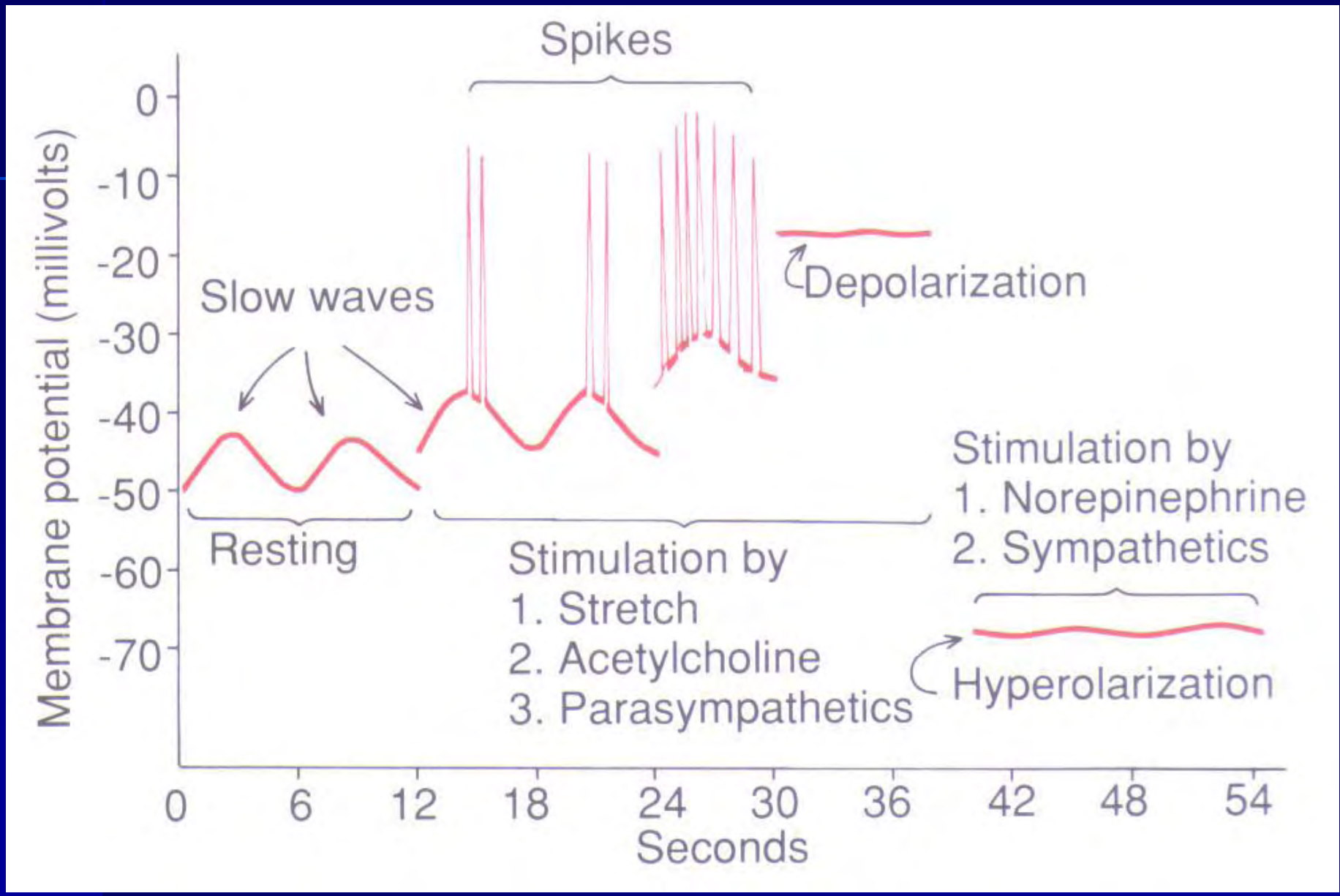
- Slow wave (basic electrical rhythm，基本电节律)
  - The spontaneous rhythmic, subthreshold depolarizations of the cell membrane (slow wave) of the gastrointestinal tract that characterizes the underlying electrical activity of the bowel （肠）
  - Initiated in the interstitial cells of Cajal (ICC) (pacemaker cell)

Santiago Ramon Y Cajal

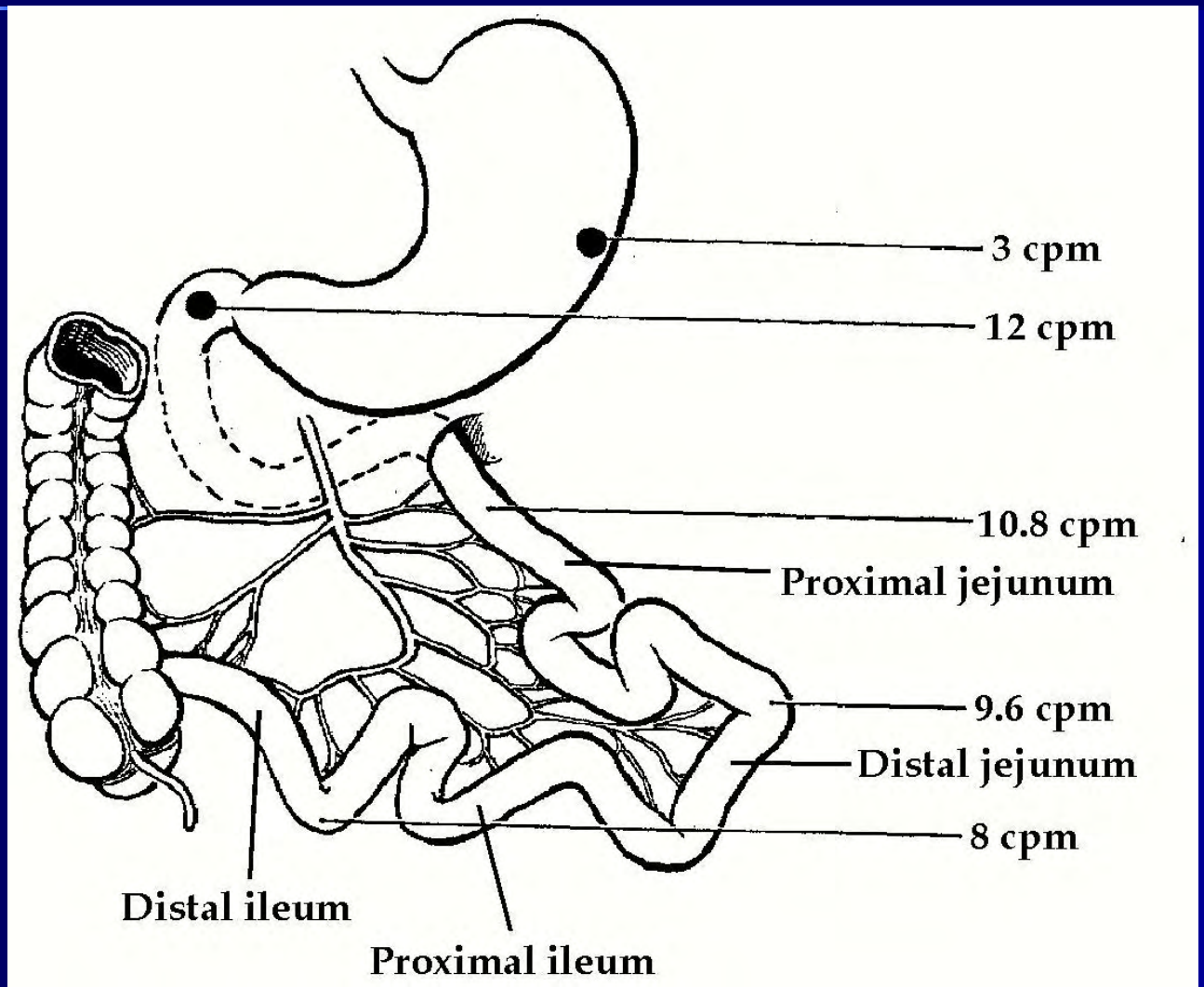
- He and Camillo Golgi received the Nobel Prize in 1906 for introduction of the silver-chromate （铬酸银） stain



- Slow wave (basic electrical rhythm,BER)
  - Intensity: 10~15 mV
  - Frequency: 3~12 cpm
  - Ionic mechanism
    - spontaneous rhythmic changes in Na^+-K^+ pump activity


Spikes
0
-10
-20
-30
-40
-50
-60
-70
Membrane potential (millivolts)
Slow waves
Depolarization
Stimulation by
1. Norepinephrine
2. Sympathetics
Resting
Stimulation by
1. Stretch
2. Acetylcholine
3. Parasympathetics
Hyperolarization
0
6
12
18
24
30
36
42
48
54
Seconds

Normal BER frequencies in the gastrointestinal system



Ileum：回肠

Jejunum：空肠

- Spike potential (Action potential)
  - Duration: 10~20 ms
  - Ionic mechanism:
    - Depolarization: Ca^{2+} influx
    - Repolarization: K^{+} efflux

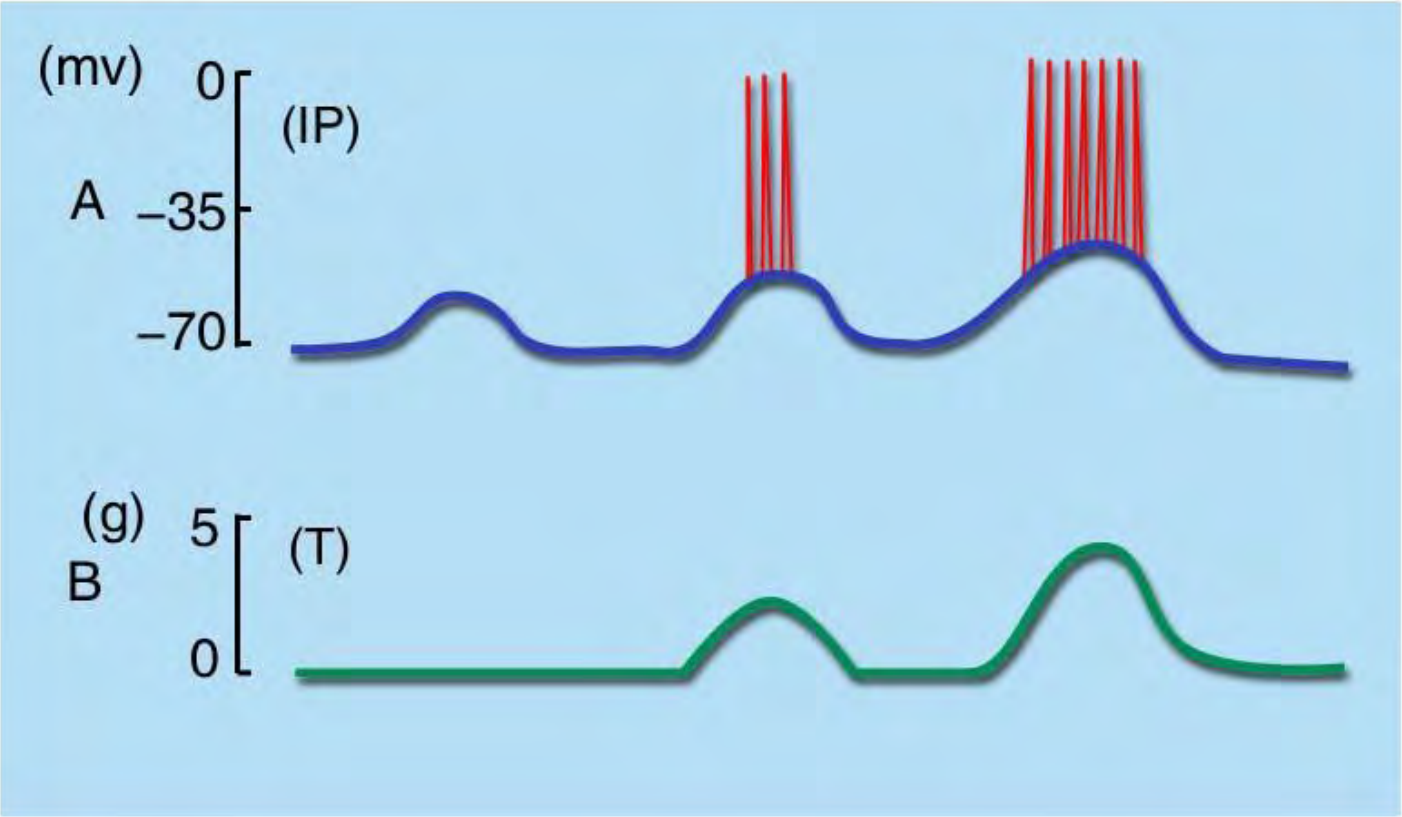
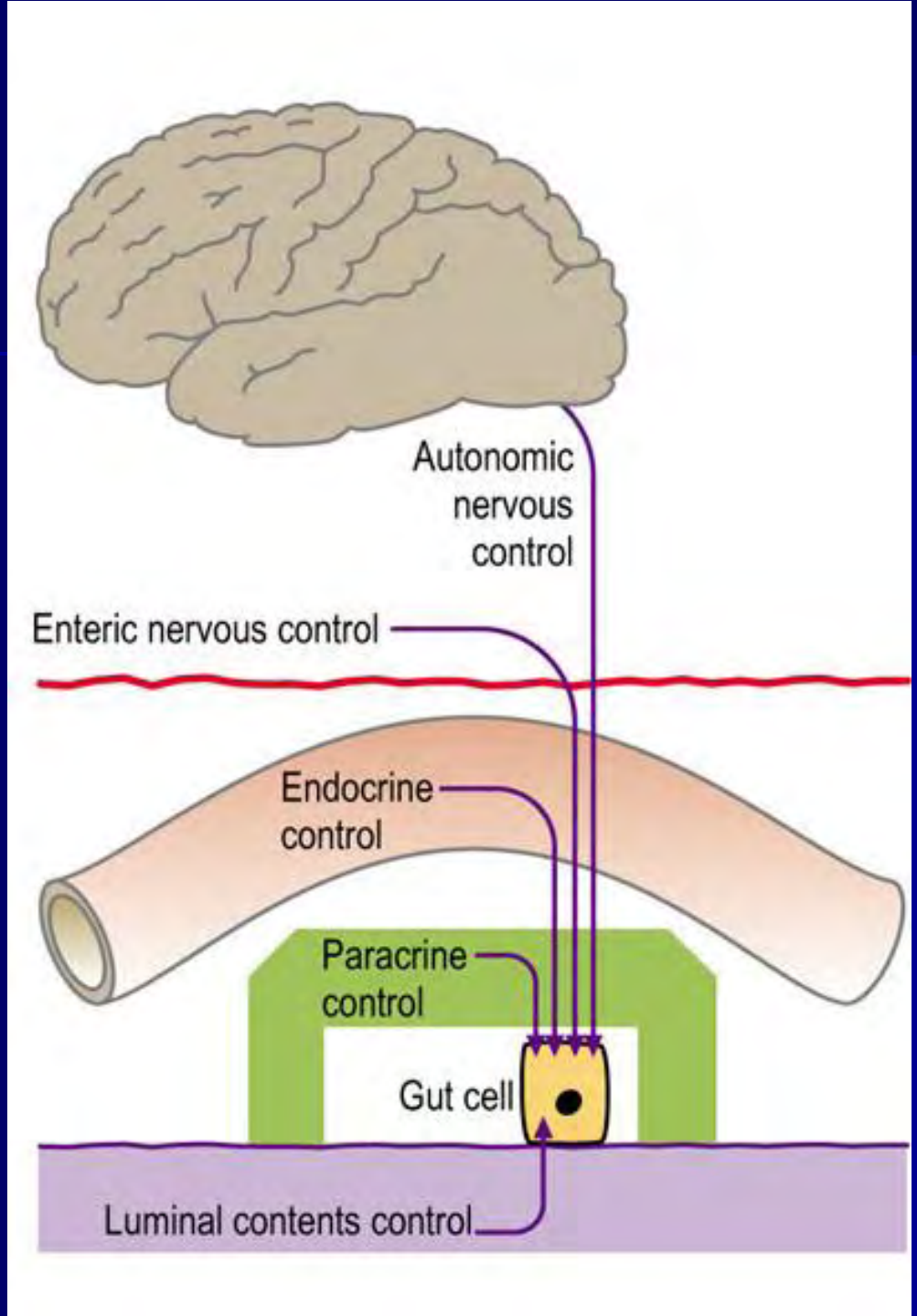


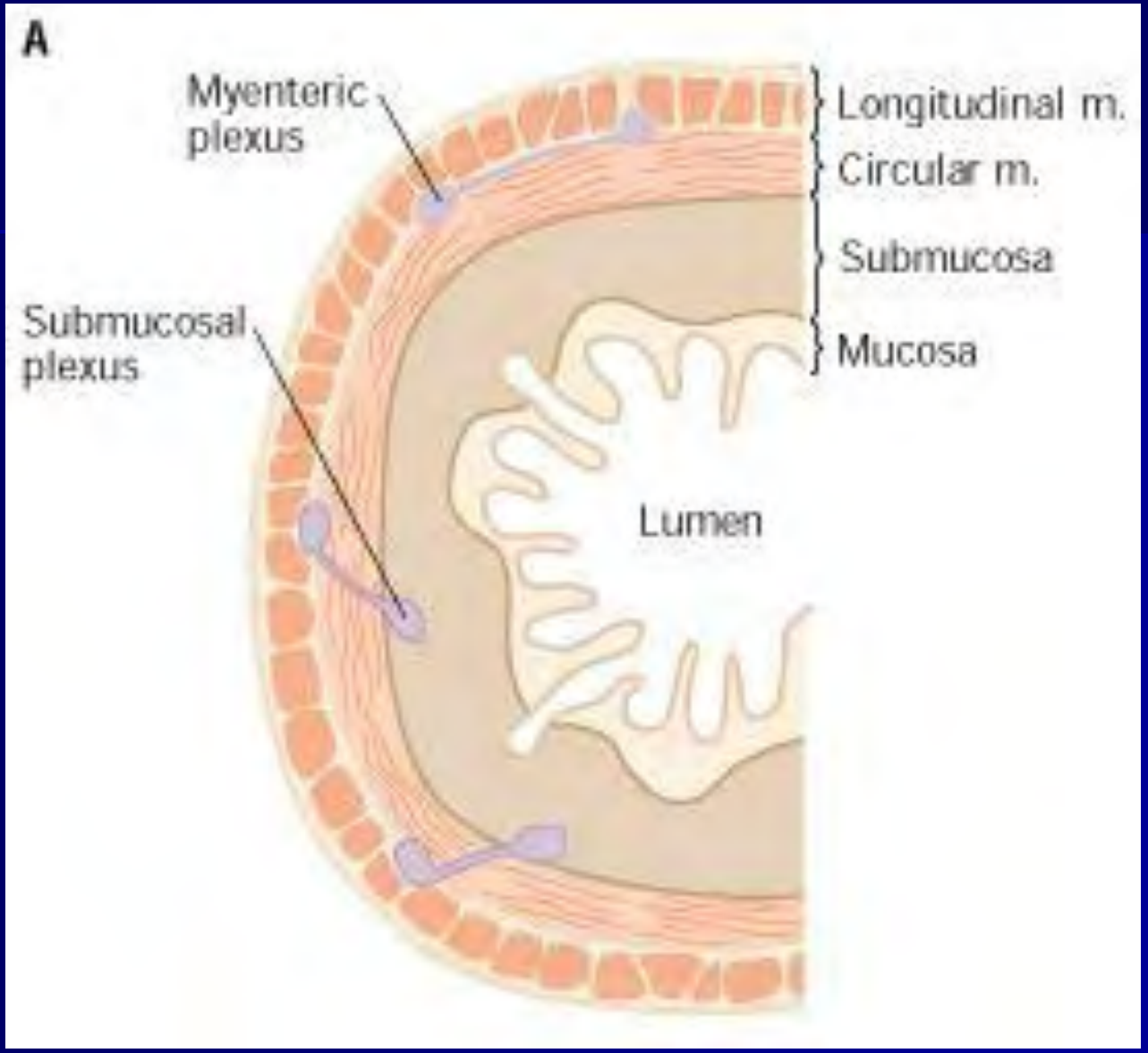
图 – 消化管平滑肌的电活动与收缩之间的关系

IP:细胞内电位 T:张力

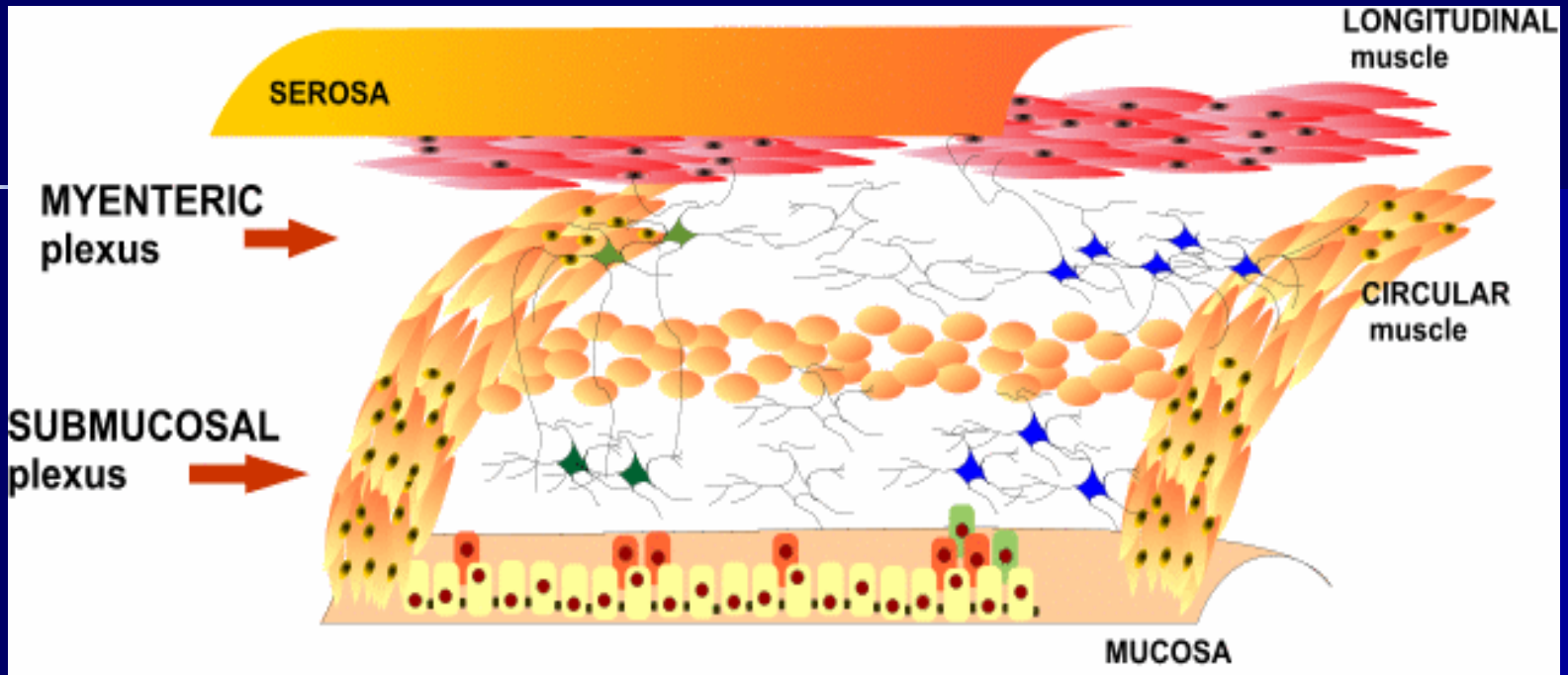
Neural control of gastrointestinal function

- Enteric nervous system (intrinsic)
- Autonomic nervous system (extrinsic)


Autonomic nervous control
Enteric nervous control
Endocrine control
Paracrine control
Gut cell
Luminal contents control


A
Myenteric plexus
Submucosal plexus
Longitudinal m.
Circular m.
Submucosa
Mucosa
Lumen

- Enteric (Intrinsic) nervous system
  - Myenteric plexus (Auerbach's plexus)
  - Submucosal plexus (Meissner's plexus)
- Neurotransmitters secreted by enteric neurons
  - Ach, NE, ATP, serotonin, dopamine, cholecystokinin（胆囊收缩素）, substance P, vasoactive intestinal polypeptide（血管活性肠肽）, somatostatin（生长抑素）, etc.



Activation of MYENTERIC PLEXUS:

- increases tonic contraction
- increases intensity of rythmic contractions
- increases rate of rythmic contractions
- increases velocity of conduction

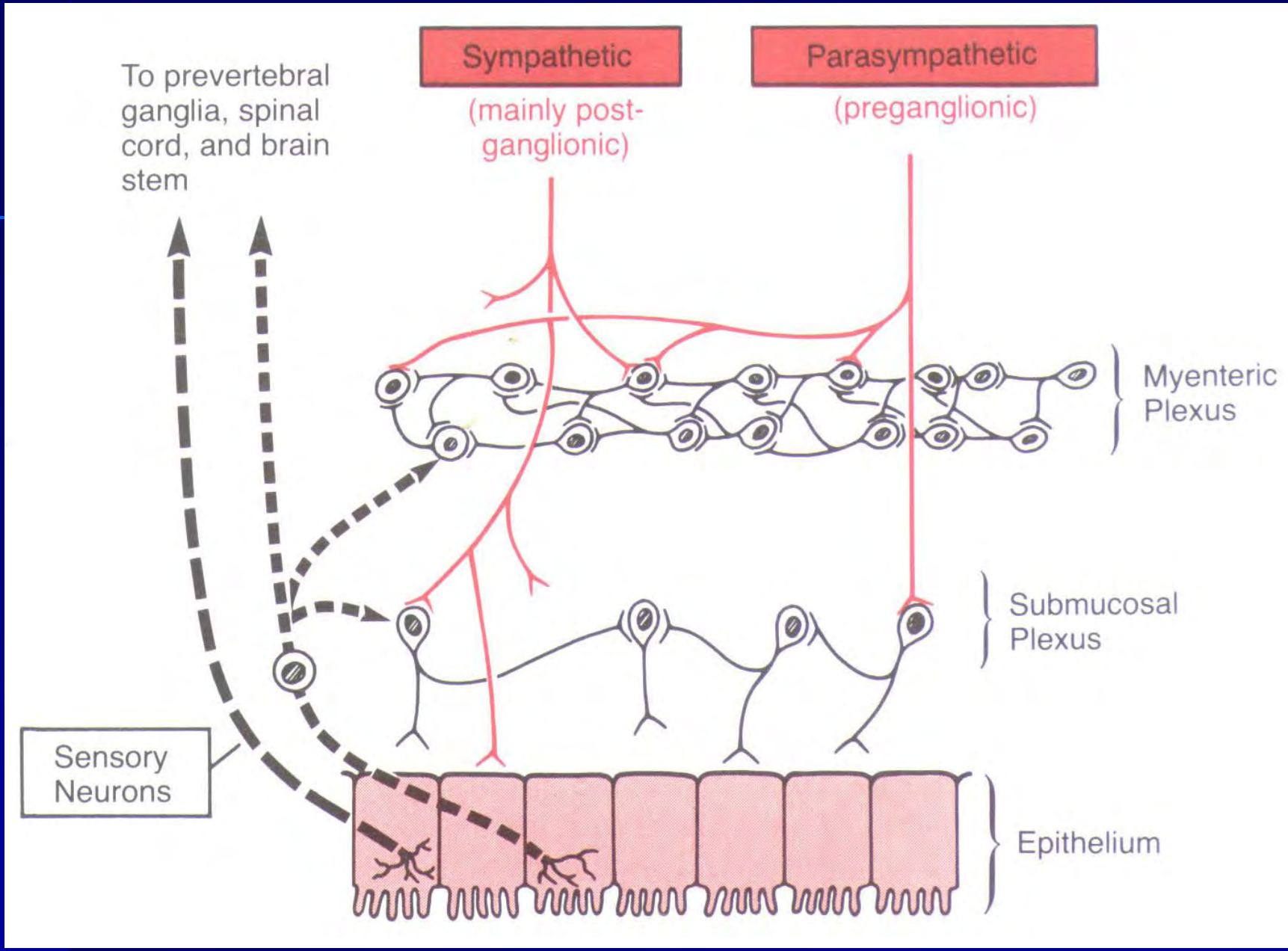
Activation of SUBMUCOSAL PLEXUS:

- increases secretory activity
- modulates intestinal absorption

- Autonomic nervous system

– Sympathetic nerve
  - NE
  - Inhibitory (-)

- Parasympathetic nerve
  - Mainly ACh
  - Stimulatory (+)


To prevertebral ganglia, spinal cord, and brain stem
Sympathetic
(mainly post-ganglionic)
Parasympathetic
(preganglionic)
Myenteric Plexus
Submucosal Plexus
Sensory Neurons
Epithelium

- Gastrointestinal reflexes
  - Three types
    - Reflexes that are integrated entirely within the enteric nervous system
    - Reflexes from the gut to the prevertebral sympathetic ganglia and then back to the gastrointestinal tract
    - Reflexes from the gut to the spinal cord or brain stem and then back to the gastrointestinal tract

Gastrointestinal hormones
（胃肠激素）

- The hormones synthesized by a large number of endocrine cells within the gastrointestinal tract
- Physiological functions
  - Control of the digestive function
  - Control of the release of other hormones
  - Trophic action

Gastrointestinal hormones

- Four main types
  - Gastrin促胃液素
  - Secretin促胰液素
  - Cholecystokinin (CCK)胆囊收缩素
  - Gastric inhibitory peptide (GIP) 抑胃肽

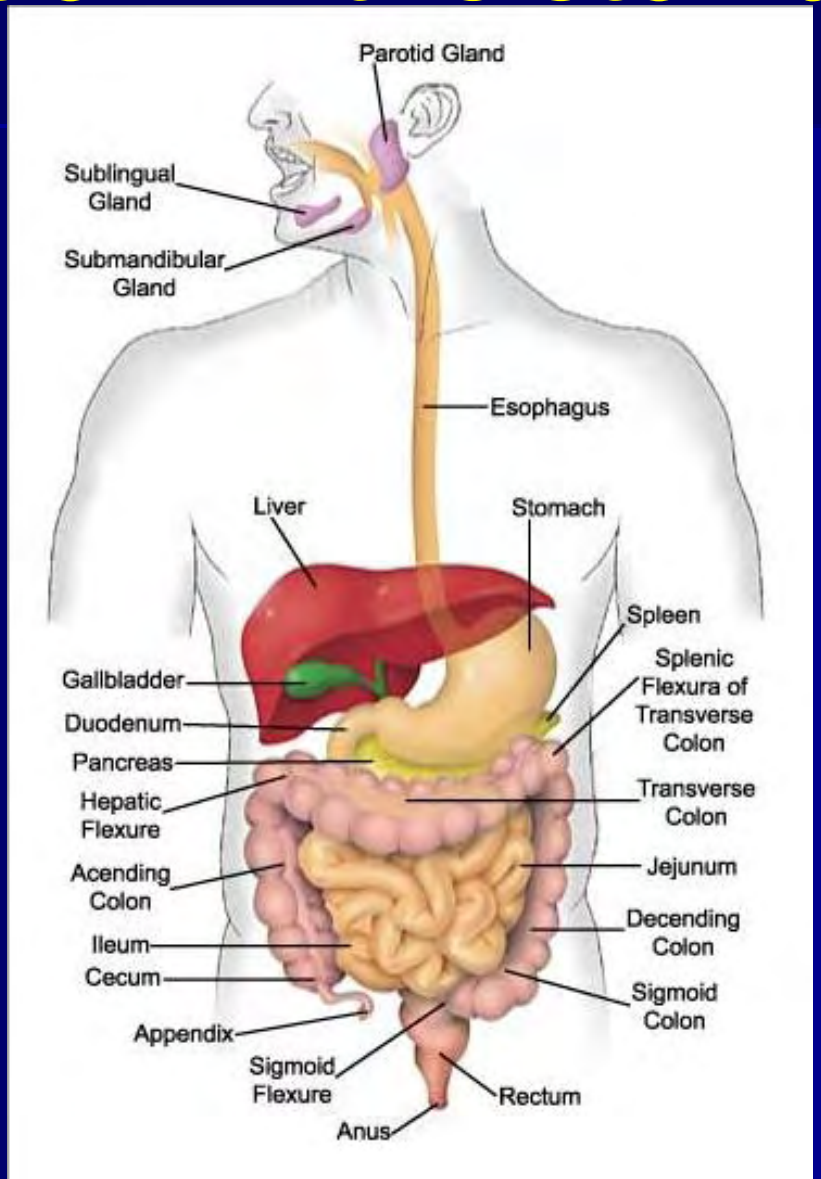
GI Peptides

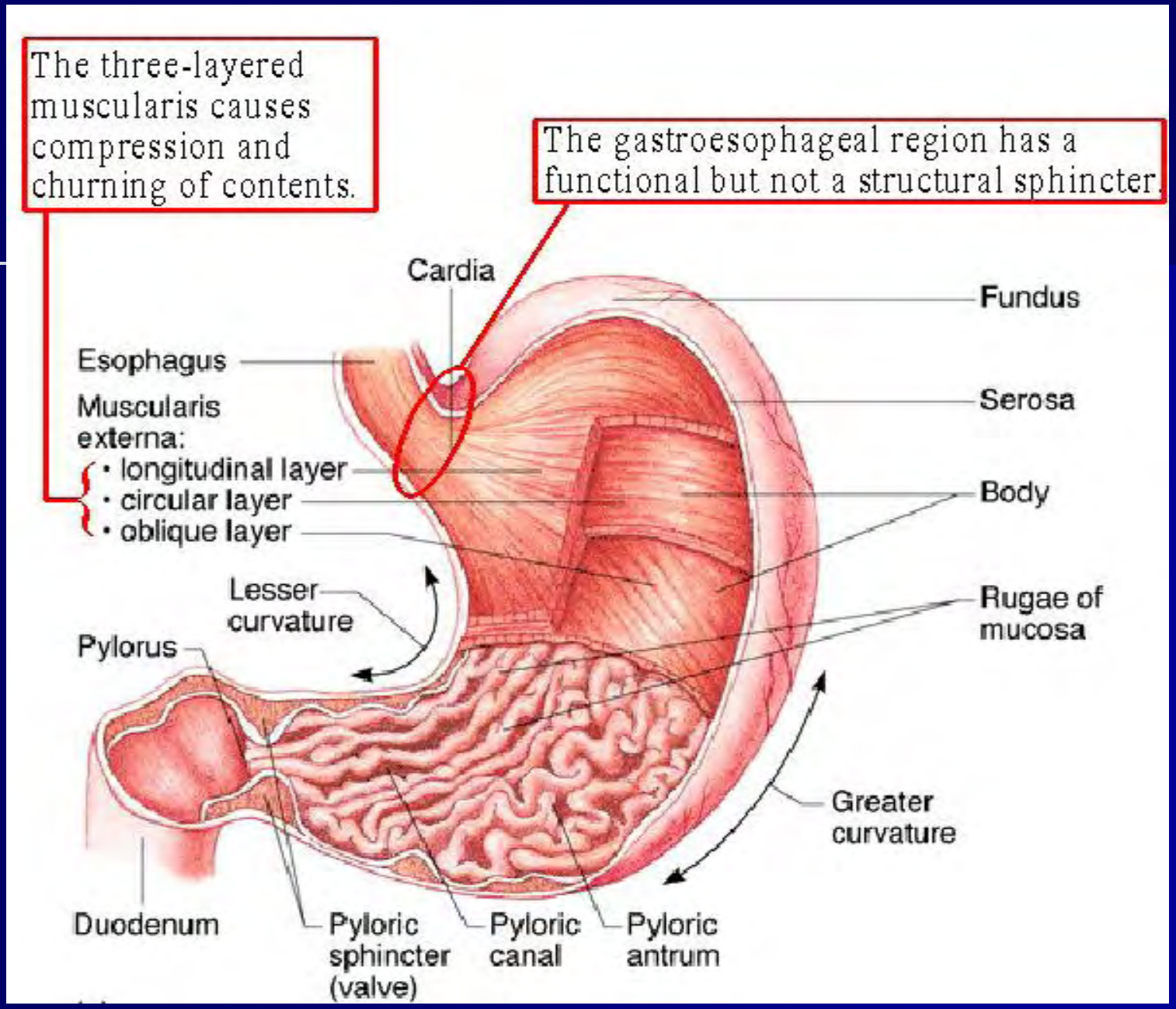
NAME	SIGNAL TRANSDUCTION MECHANISM	GI EFFECT	CNS EFFECT
CCK (2) (cholecystokinin)	IP_3/DAG	Regulation of food intake; satiety	May be involved in etiology of anxiety
VIP (2) (vasoactive intestinal peptide)	↑cAMP	Relaxation of tracheal smooth muscle; involved in intestinal transport	
Somatostatin (5)	↓cAMP; misc other effects	Found in gastric and duodenal mucosa	Primary function is control of activity of growth hormone releasing hormone
Neurotensin (1)	IP_3/DAG, Ca^{2+}, ↓cAMP	Found in intestinal mucosa	
Substance P/ tachykinin (1)	IP_3/DAG	Contracts smooth muscle of gut	Proposed to be a sensory neurotransmitter associated with pain transmssion
Bradykinin (2)	IP_3/DAG	Produces slow contraction of gut	

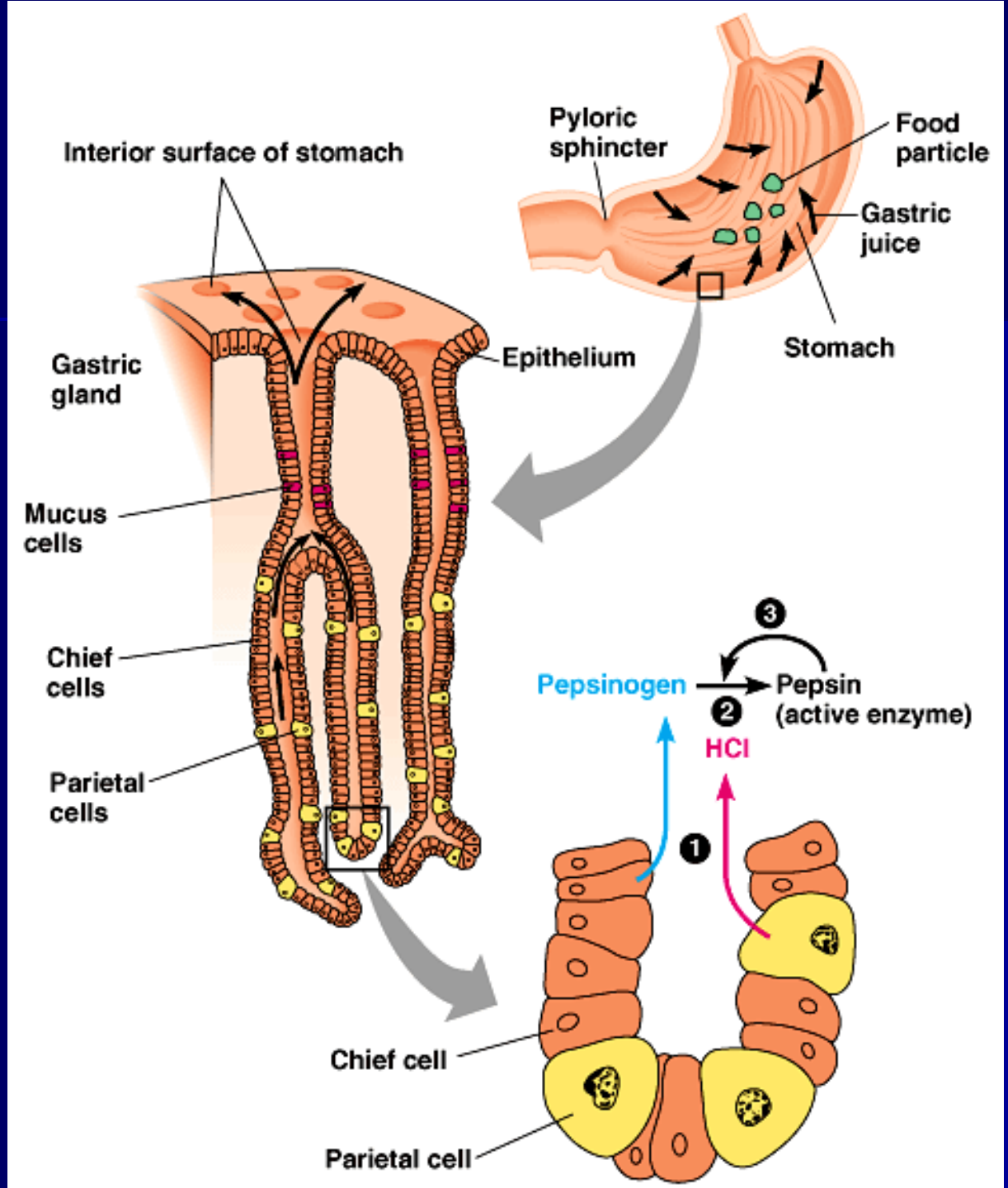
Brain-gut peptide（脑-肠肽）

- Definition:
  - the peptide which is found in the brain and the gut also.
- Classification:
  - Gastrin促胃液素
  - CCK
  - P substance

Digestion in the stomach




The three-layered muscularis causes compression and churning of contents.
The gastroesophageal region has a functional but not a structural sphincter.
Cardia
Fundus
Esophagus
Serosa
Muscularis externa:
• longitudinal layer
• circular layer
• oblique layer
Body
Lesser curvature
Rugae of mucosa
Pylorus
Greater curvature
Duodenum
Pyloric sphincter (valve)
Pyloric canal
Pyloric antrum

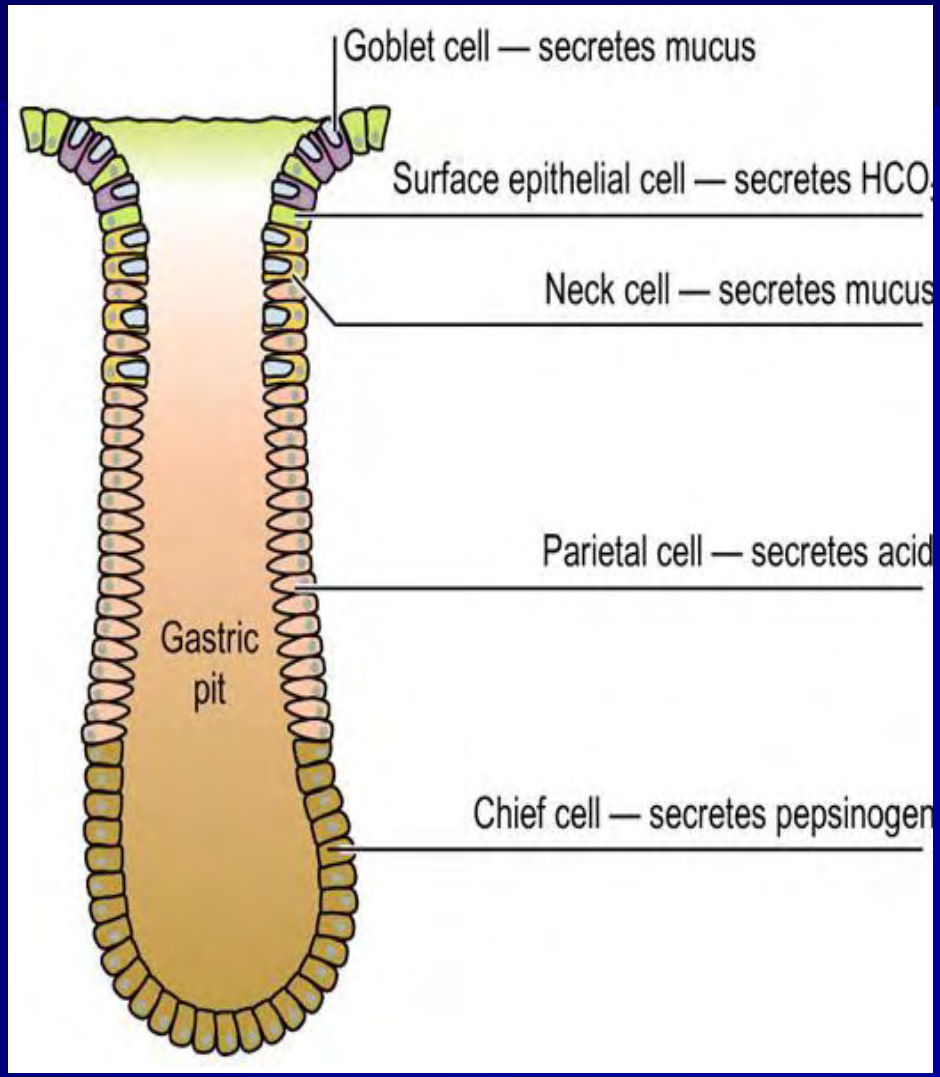

Interior surface of stomach
Pyloric sphincter
Food particle
Gastric juice
Stomach
Gastric gland
Epithelium
Mucus cells
Chief cells
Parietal cells
3
Pepsinogen
Pepsin (active enzyme)
2
HCl
1
Chief cell
Parietal cell

Gastric juice（胃液）

- Properties
  - pH 0.9~1.5
  - 1.5~2.5 L/day
- Major components
  - Hydrochloric acid 盐酸
  - Pepsinogen 胃蛋白酶原
  - Mucus 粘液
  - Intrinsic factor 内因子

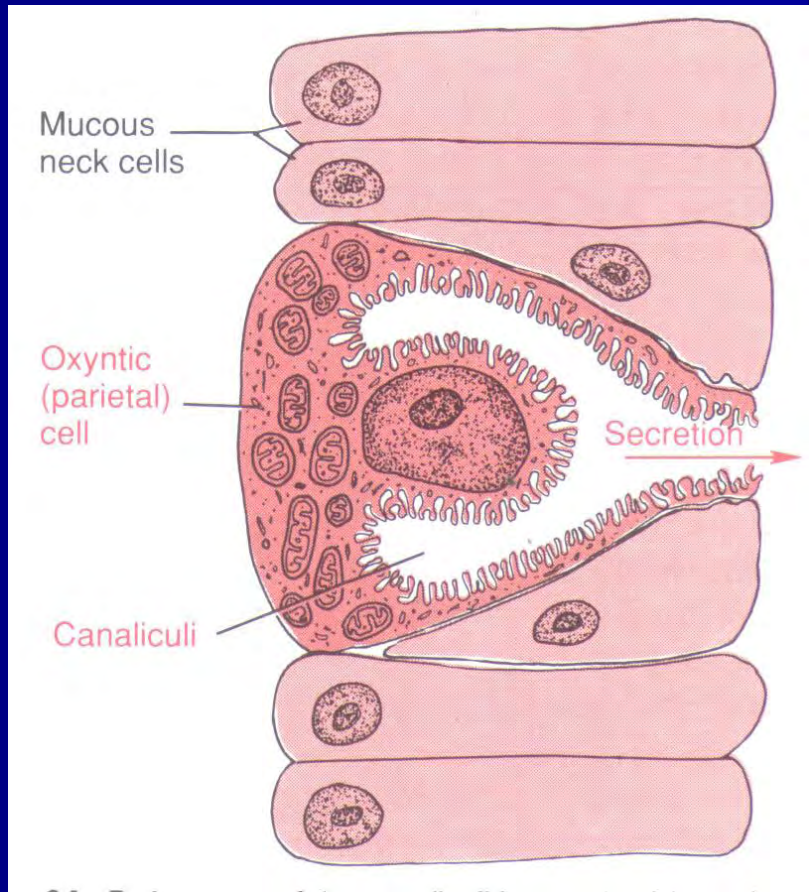
Gastric juice

- Secreted by
  - parietal cells壁细胞
  - Chief cells主细胞
  - Mucous neck cells粘液颈细胞



Hydrochloric acid

- Secreted by the parietal cells
- Output
  - Basal: 0~5 mmol/h
  - Maximal: 20~25 mmol/h



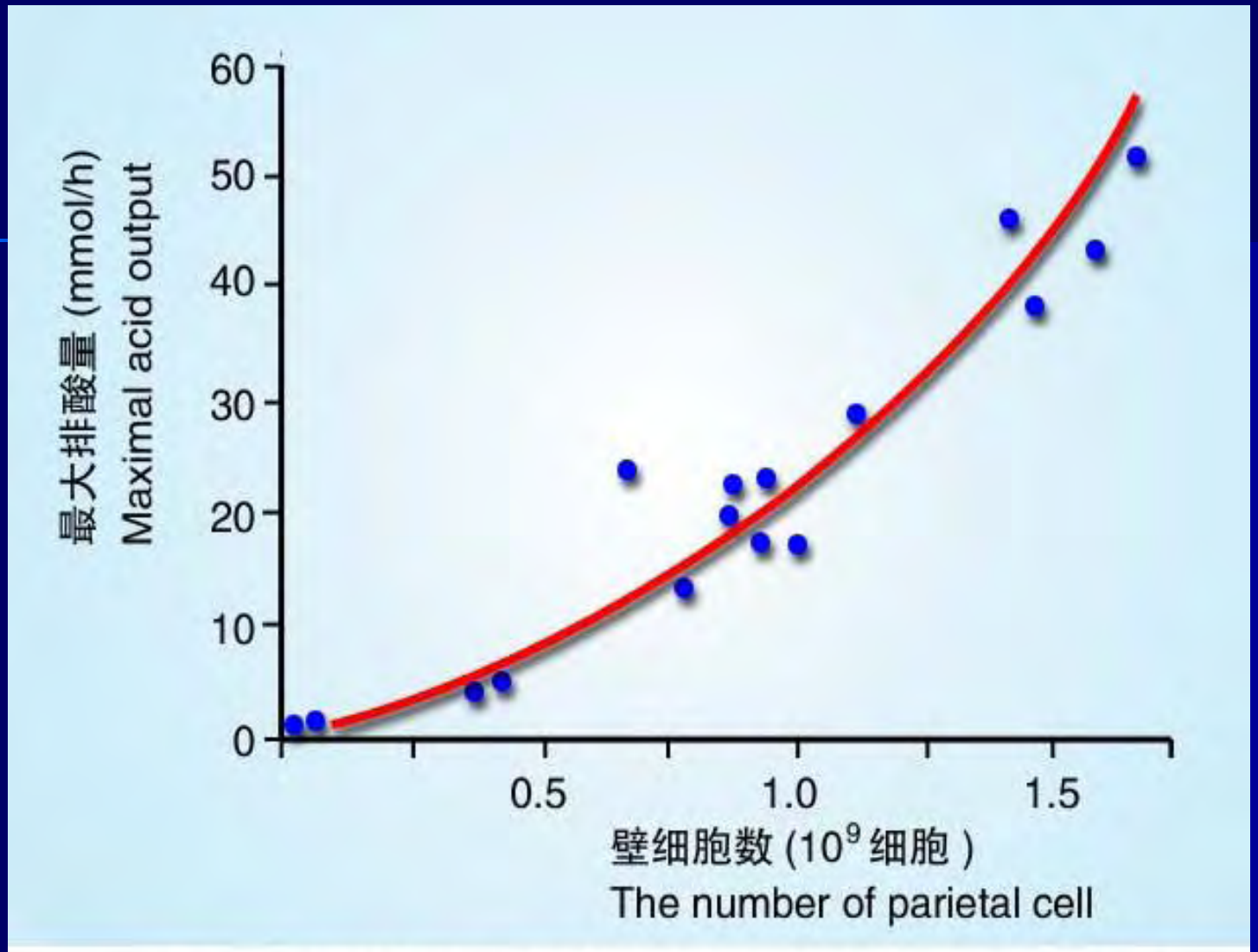
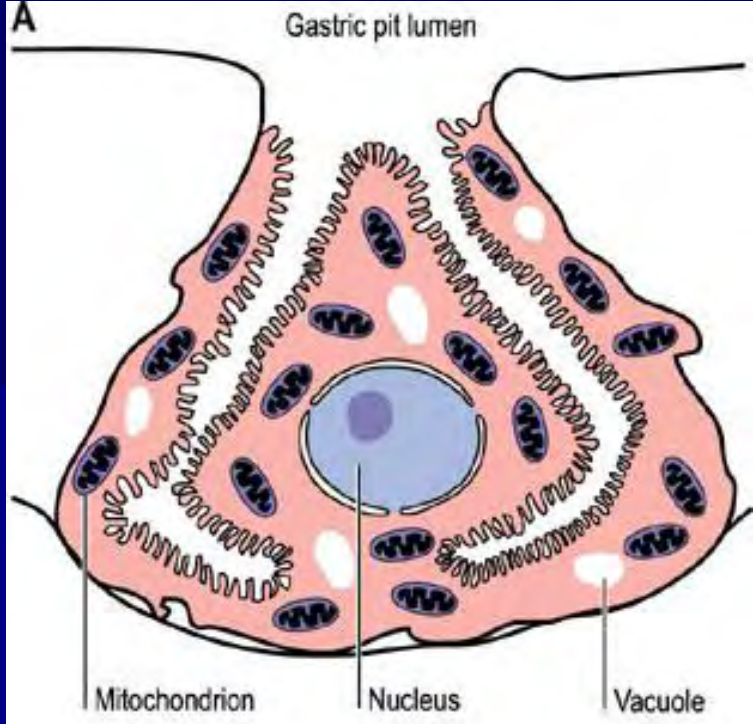
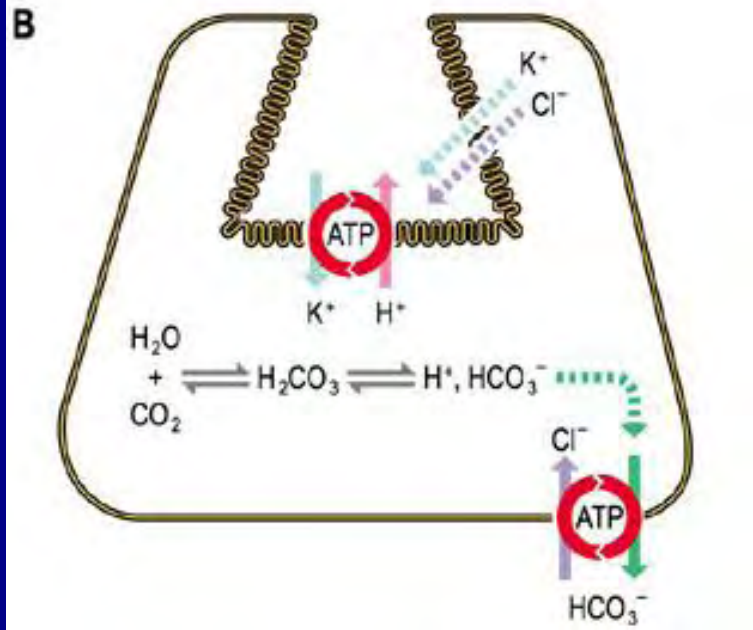
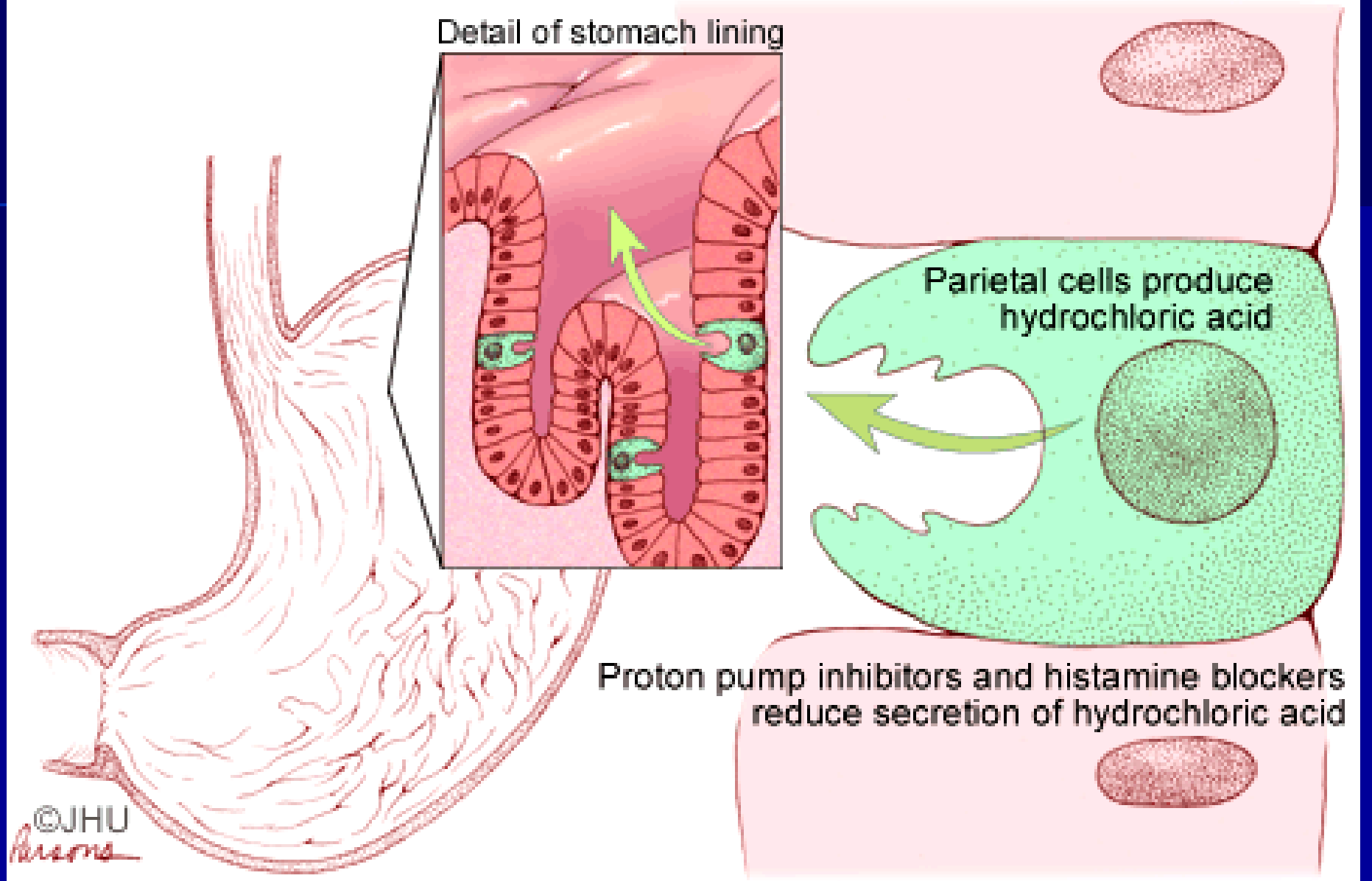


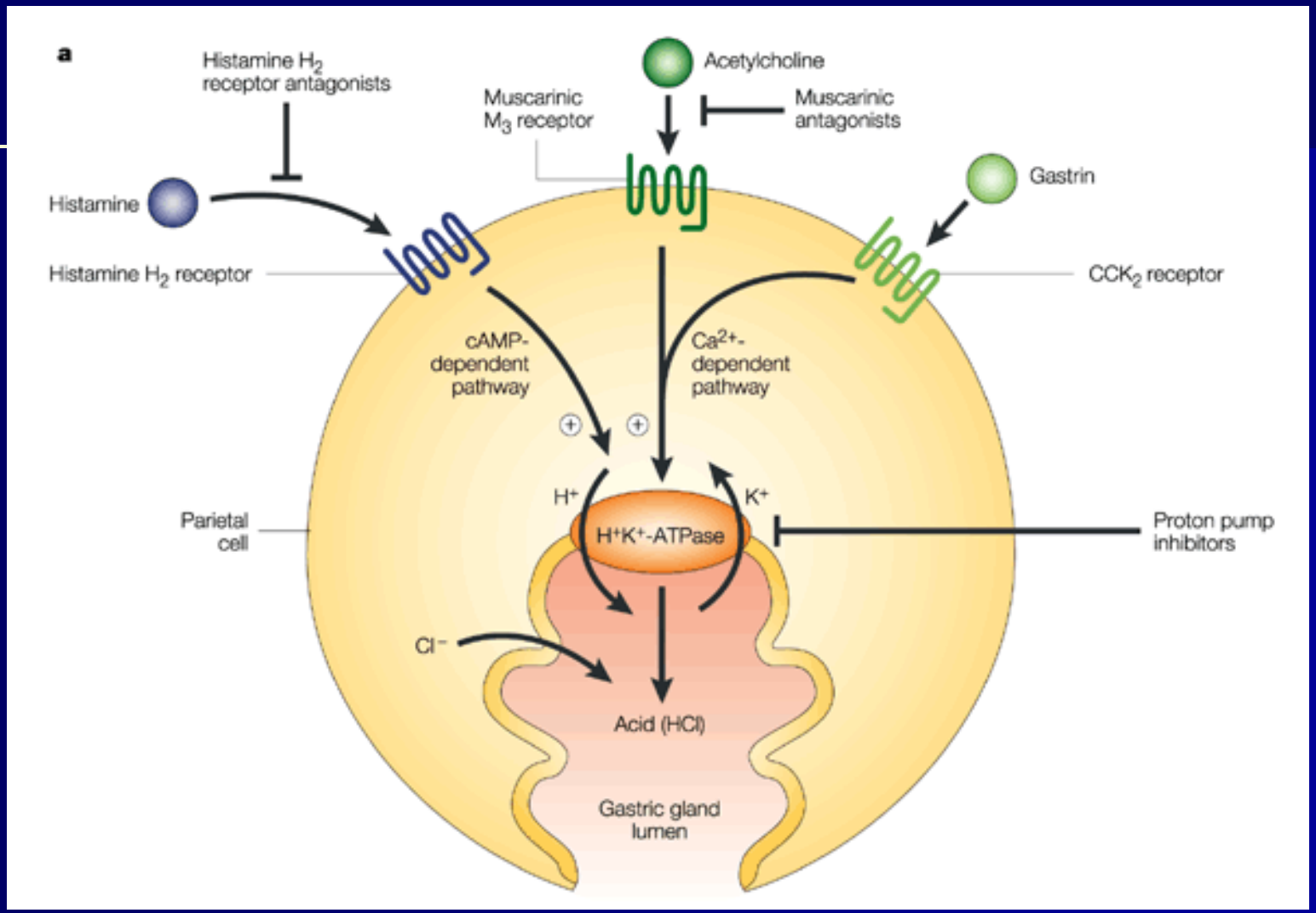
图 – 胃酸最大排出量与壁细胞数目的关系

- Mechanism of HCl secretion
  - Active transport
  - H^+ pump (proton pump)
  - Cl^+-HCO_3^- exchange





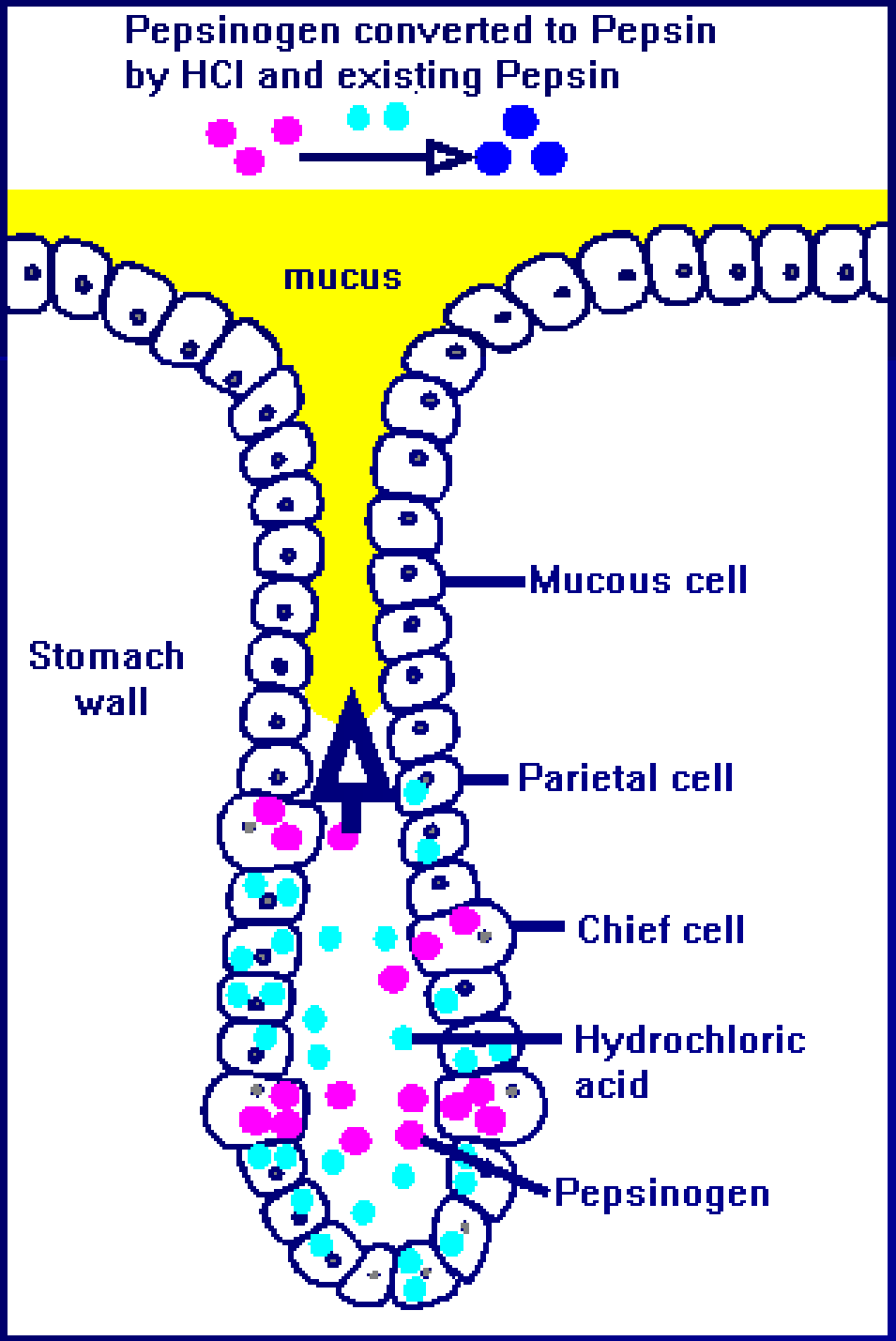

Detail of stomach lining
Parietal cells produce hydrochloric acid
Proton pump inhibitors and histamine blockers reduce secretion of hydrochloric acid
©JHU


a
Histamine H_2 receptor antagonists
Acetylcholine
Muscarinic M_3 receptor
Muscarinic antagonists
Gastrin
Histamine
Histamine H_2 receptor
CCK_2 receptor
cAMP-dependent pathway
Ca^{2+}-dependent pathway
H^+
K^+
Parietal cell
H^+K^+-ATPase
Proton pump inhibitors
Cl^-
Acid (HCl)
Gastric gland lumen

- Role of HCl
  - Acid sterilization 杀菌
  - Activation of pepsinogen
  - Promotion of secretin促胰液素secretion
  - Assisted effect of iron and calcium absorption

Pepsinogen

- MW: 42,500
- Secreted by the chief cells as an inactive precursor of pepsin
- Activated in the stomach, initially by H^+ ions and then by active pepsin, autocatalytic activation
- Active *pepsin* (MW: 35,000)

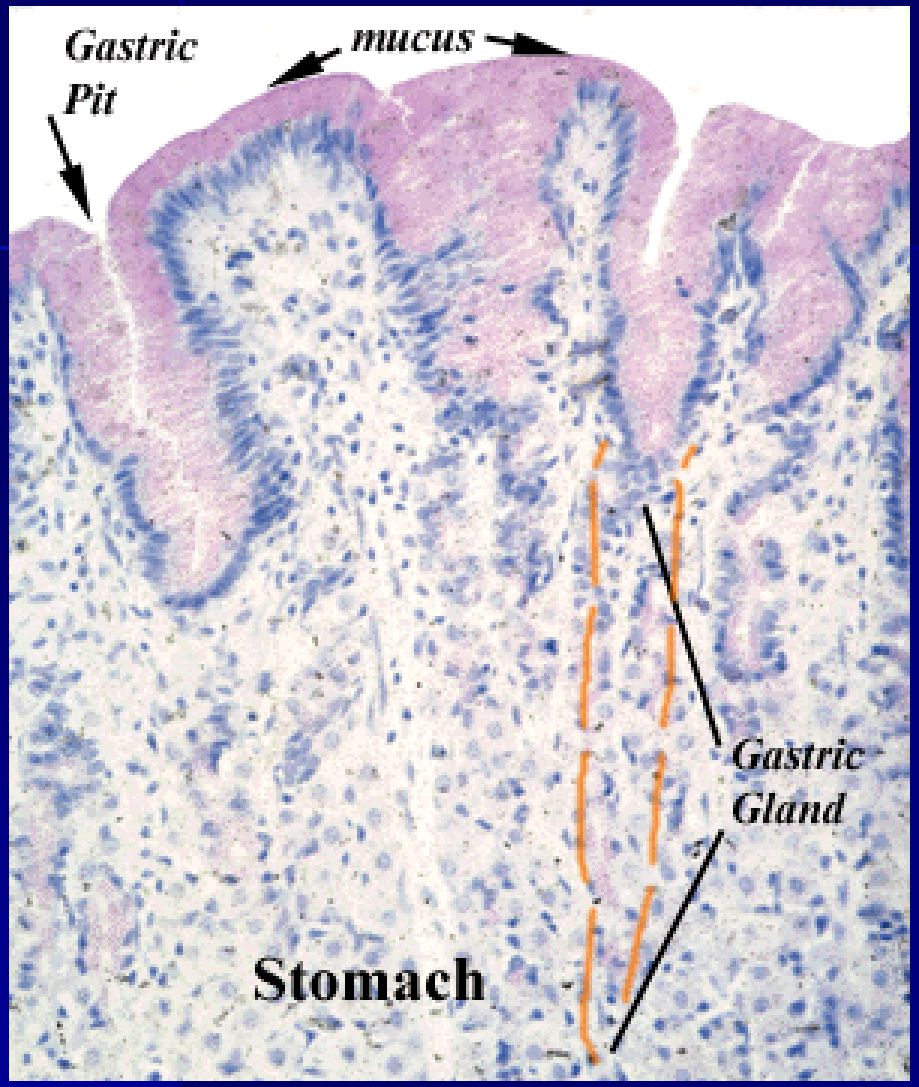

Pepsinogen converted to Pepsin
by HCl and existing Pepsin
mucus
Mucous cell
Stomach
wall
Parietal cell
Chief cell
Hydrochloric
acid
Pepsinogen

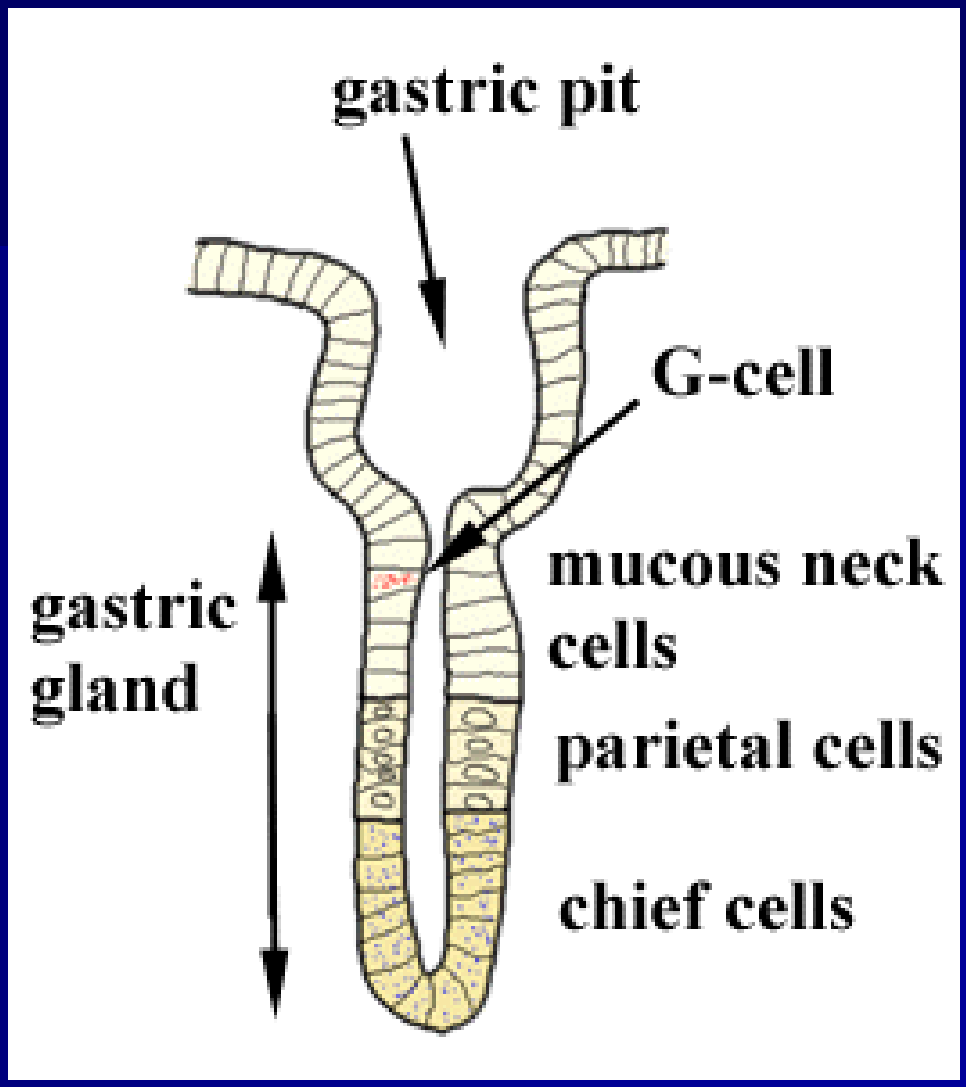
- Effect of pepsin

  Pepsin is an endopeptidase, which attacks peptide bonds in the interior of large protein molecules

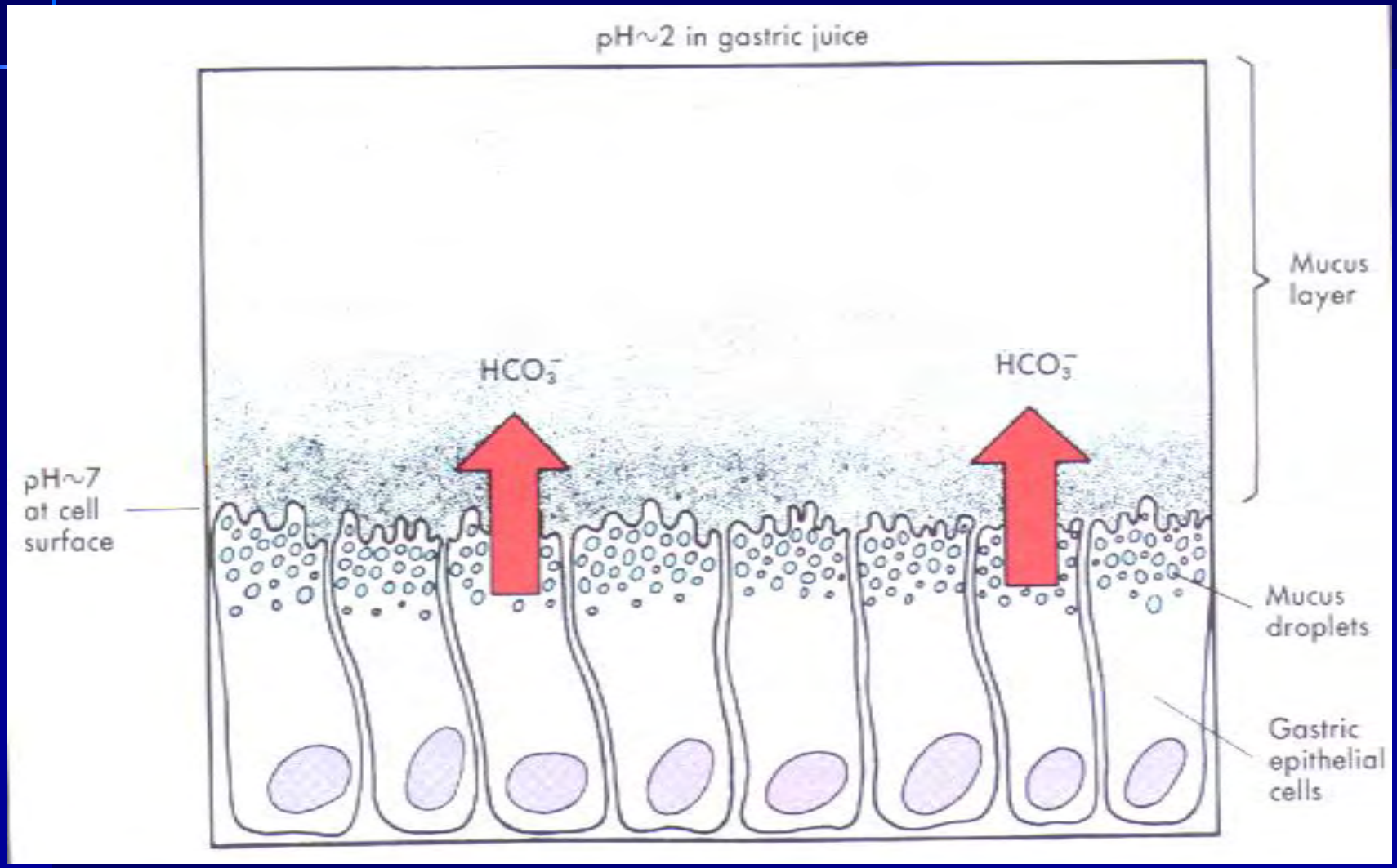
Mucus

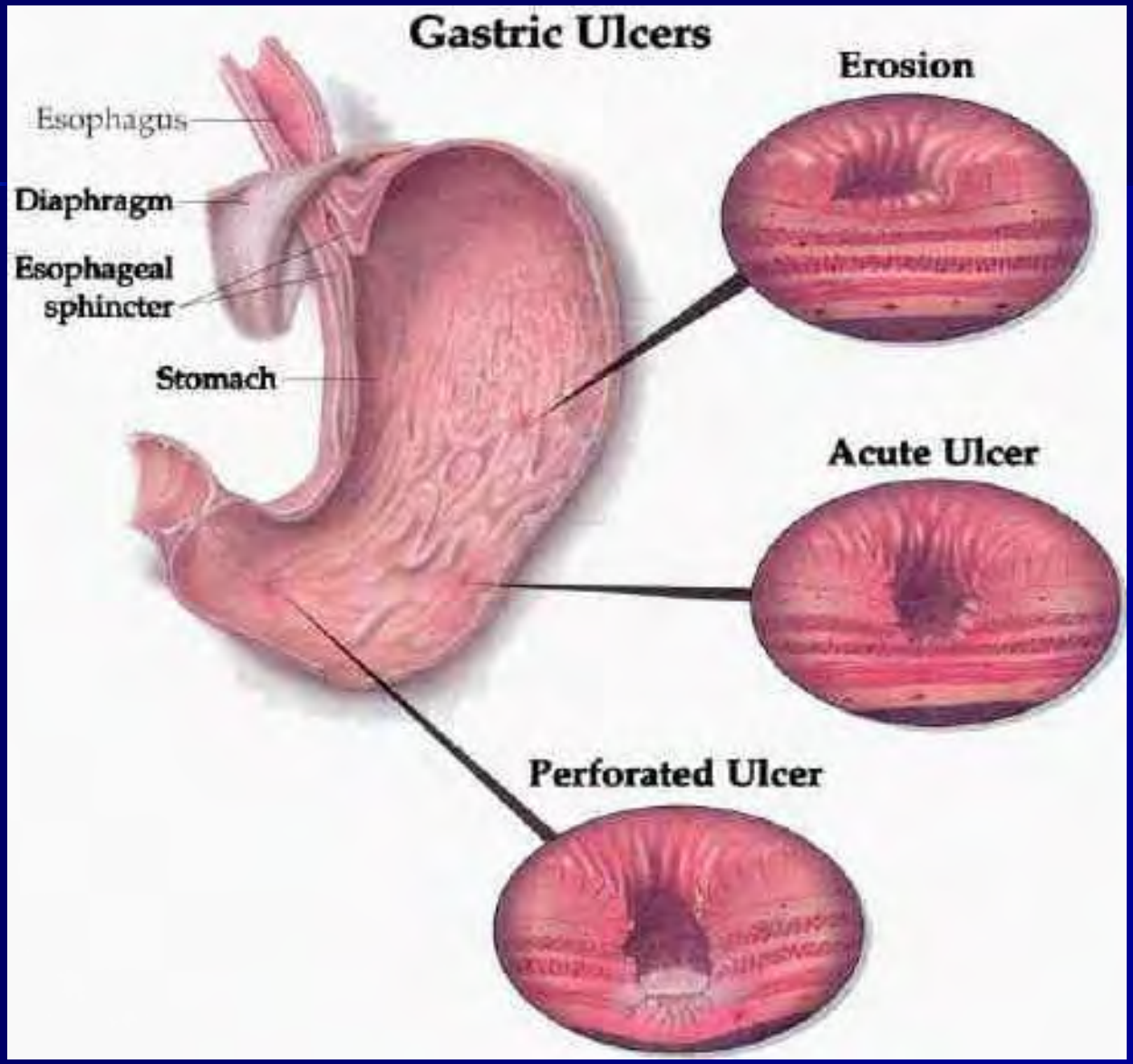
- Secreted by the epithelial cells all over the mucosa and by the neck mucus cells in the upper portion of the gastric glands and pyloric glands
- Role
  - Lubrication of the mucosal surface
  - Protection of the tissue from mechanical damage by food particles


Gastric
Pit
mucus
Gastric
Gland
Stomach


gastric pit
G-cell
gastric
gland
mucous neck
cells
parietal cells
chief cells

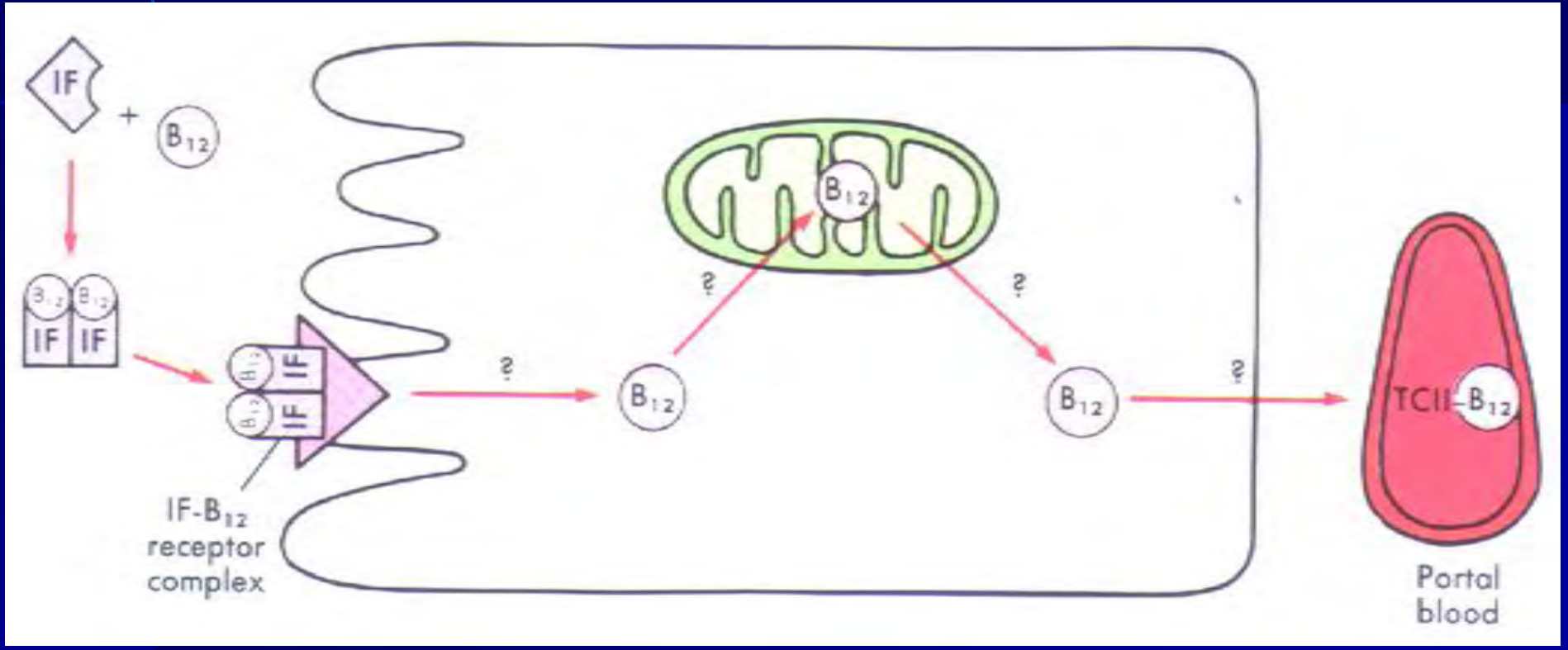
Mucus-HCO_3^- barrier




Gastric Ulcers
Erosion
Esophagus
Diaphragm
Esophageal sphincter
Stomach
Acute Ulcer
Perforated Ulcer

Intrinsic factor

- A high molecular weight glycoprotein, synthesized and secreted by the parietal cells
- The intrinsic factor binds to Vit B_{12} and facilitates its absorption


IF
+
B_{12}
IF
IF
IF
IF
IF-B_{12} receptor complex
?
B_{12}
?
B_{12}
?
B_{12}
?
TCII-B_{12}
Portal blood

Regulation of gastric secretion

- Basic factors that stimulate gastric secretion
  - Acetylcholine (+ all secretory cells)
  - Gastrin (+ parietal cells)
  - Histamine (+ parietal cells)

Regulation of gastric secretion

- Nervous regulation
  - 'Short' reflex pathways
    - 'Short' excitatory reflexes: mediated by cholinergic neurons in the plexuses
    - 'Short' inhibitory reflexes: mediated by non-adrenergic non-cholinergic (NANC) neurons

Regulation of gastric secretion

- Nervous regulation
  - 'Long' autonomic pathways
    - 'Long' excitatory reflexes: parasympathetic
    - 'Long' inhibitory pathways: sympathetic

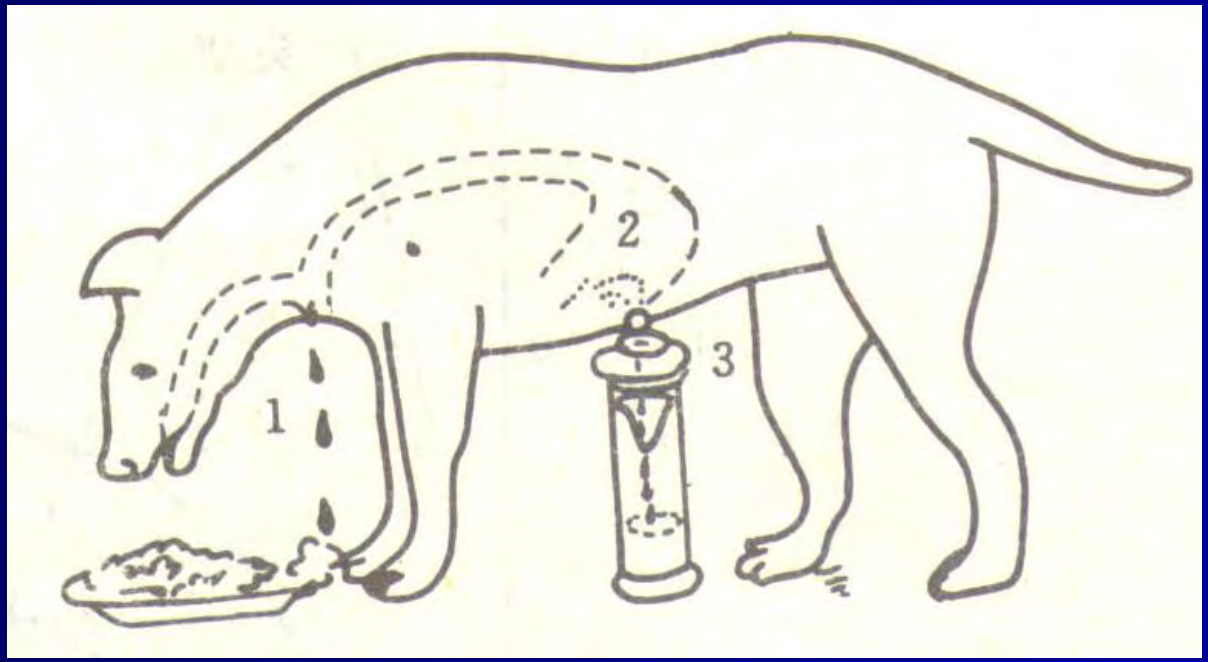
Regulation of gastric secretion

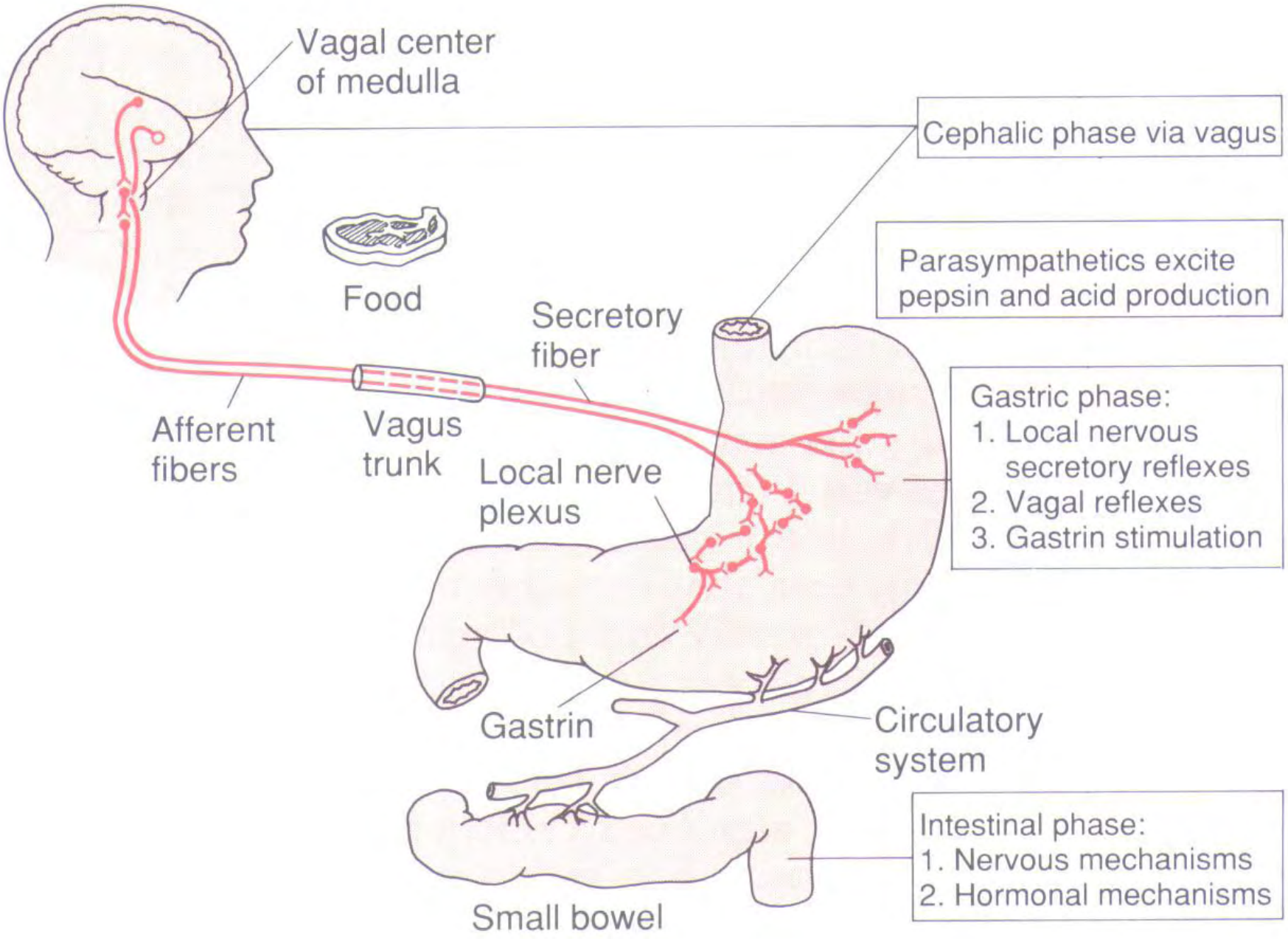
- Humoral regulation

Excitatory	Inhibitory
ACh	Somatostatin
Histamine	Secretin
Gastrin	5-hydroxytryptamine (5-HT)
	Prostaglandin前列腺素

Phases of gastric secretion

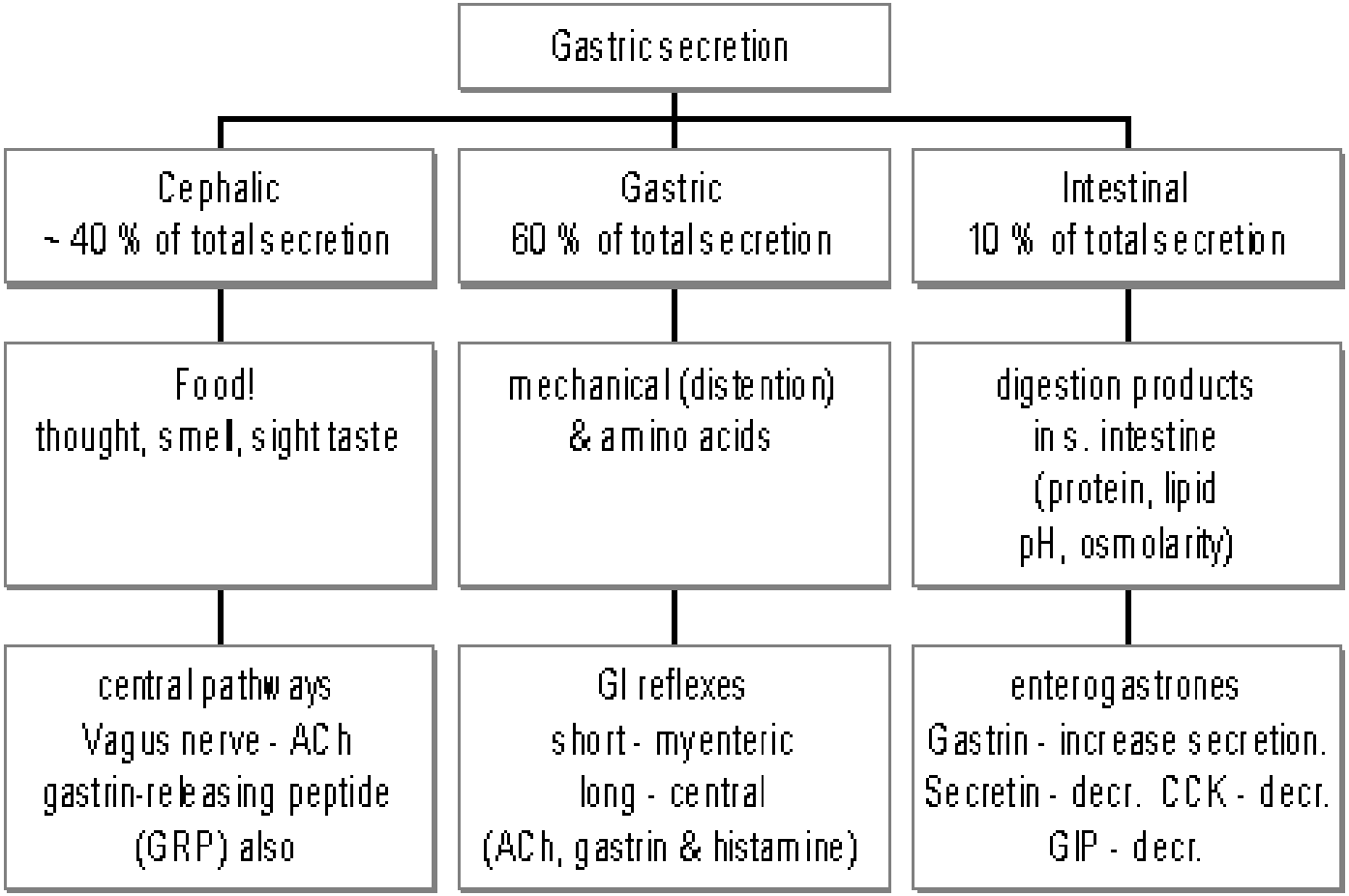
- Cephalic phase 头相
- Gastric phase 胃相
- Intestinal phase 肠相




Vagal center of medulla
Cephalic phase via vagus
Food
Parasympathetics excite pepsin and acid production
Secretory fiber
Afferent fibers
Vagus trunk
Local nerve plexus
Gastric phase:
1. Local nervous secretory reflexes
2. Vagal reflexes
3. Gastrin stimulation
Gastrin
Circulatory system
Intestinal phase:
1. Nervous mechanisms
2. Hormonal mechanisms
Small bowel

Control of gastric secretion

Phases of gastric secretion



November 1999

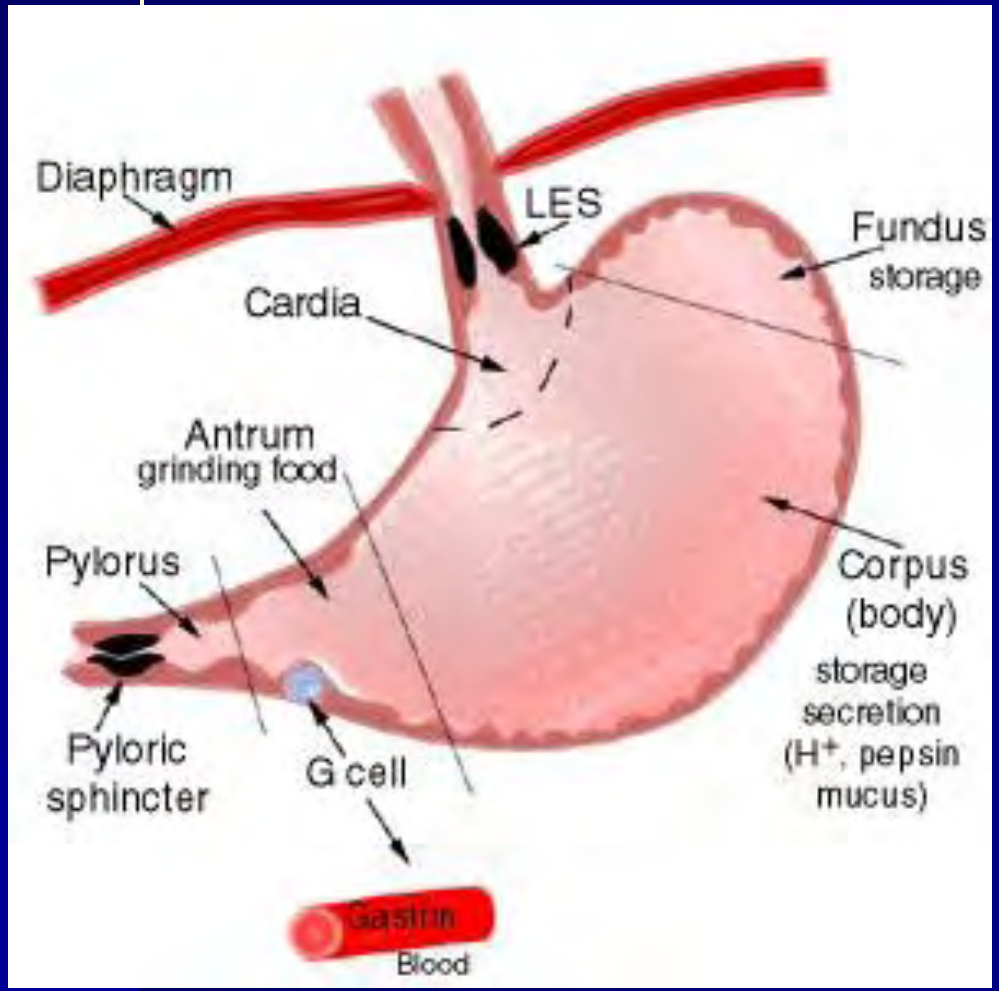
Inhibition of gastric secretion

The functional purpose of the inhibition of gastric secretion by intestinal factors is presumably to slow the release of chyme 食糜 from the stomach when the small intestine is already filled or overactive

Inhibition of gastric secretion

- Reverse enterogastric reflex: initiated by the presence of food in the small intestine
- Secretin secretion: stimulated by the presence of acid, fat, protein breakdown products, hyperosmotic or hypo-osmotic fluids, or any irritating factors in the upper small intestine

Motor function of the stomach



Proximal stomach

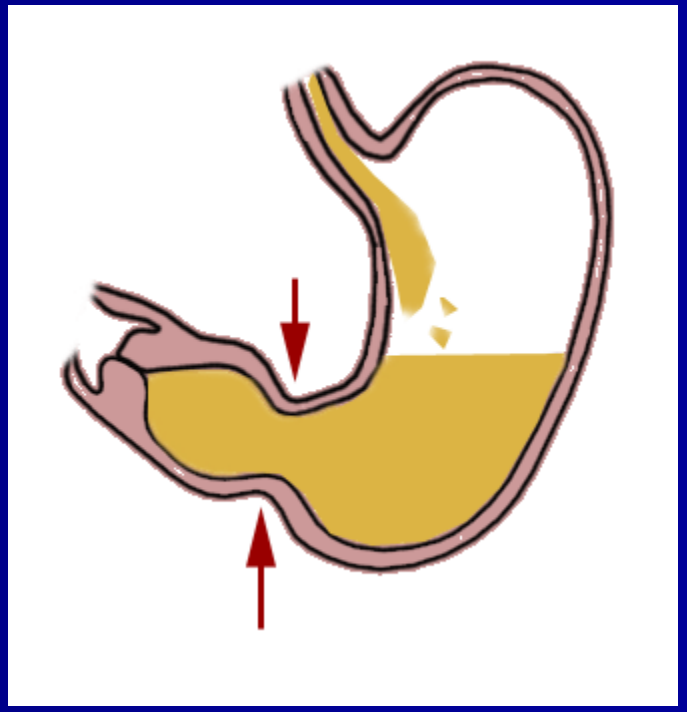
- cardia 贲门
- fundus 胃底
- corpus (body)胃体

Distal stomach

- antrum 胃窦
- pylorus 幽门
- pyloric sphincter 幽门括约肌

Motor function of the stomach

- Receptive relaxation 容受性舒张
  - Storage function (1.0~1.5 L)
  - Vago-vagal reflex
- Peristalsis 蠕动
  - BER in the stomach



Contractions in the empty stomach

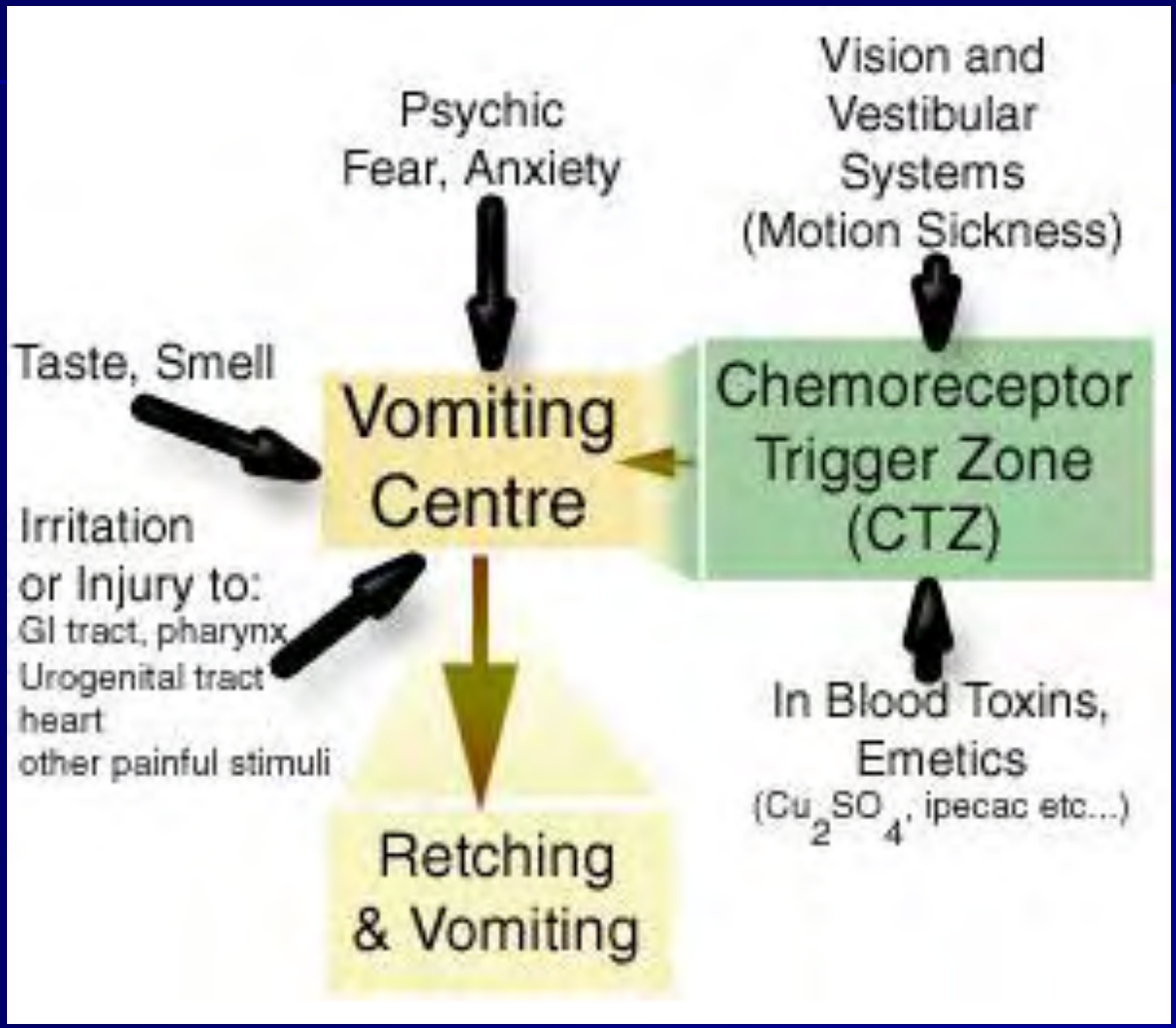
- Migrating Motor Complex (移行性运动综合波, MMC)
  - Periodic waves of contraction, which move along the gastrointestinal tract from stomach to colon
  - Purpose of this activity: to 'sweep' debris out of the digestive tract during the interdigestive period
  - MMCs can lead to hunger contractions, which are associated with discomfort, referred to as 'hunger pains'

Emptying of the stomach排空

- Emptying rate
  - Small particle > large particle
  - Isosmotic > hyper- & hypo-osmotic
  - Carbohydrates > Protein > Fat
  - Regular meal 4～6 hrs

- Regulation of stomach emptying
  - Gastric factors that promote emptying
    - Gastric food volume
    - Gastrin
  - Duodenal factors that inhibit stomach emptying
    - Enterogastric nervous reflexes
    - Fat
    - Cholecystokinin

Vomiting


Psychic
Fear, Anxiety
Vision and
Vestibular
Systems
(Motion Sickness)
Taste, Smell
Vomiting
Centre
Chemoreceptor
Trigger Zone
(CTZ)
Irritation
or Injury to:
GI tract, pharynx
Urogenital tract
heart
other painful stimuli
In Blood Toxins,
Emetics
(Cu_2SO_4, ipecac etc...)
Retching
& Vomiting